NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ASTRAZENECA AB, AKEIEBOLAGET HÄSSLE, ASTRAZENECA LP, and ZENECA INC. Plaintiffs, v. ANDRX LABS, LLC, ANDRX CORPORATION, and ACTAVIS, INC., Defendants.	CIVIL ACTION NO. 14-8030 (MLC)(DEA)
ASTRAZENECA AB, AKEIEBOLAGET HÄSSLE, ASTRAZENECA LP, and ZENECA INC. Plaintiffs, v. PERRIGO COMPANY PLC, PERRIGO COMPANY, and L. PERRIGO COMPANY, Defendants.	CIVIL ACTION NO. 15-1057 (MLC)(DEA) **MEMORANDUM OPINION**

Cooper, District Judge

OUTLINE

PRELIMINARY STATEMENT

This is a claim construction opinion in two related but not consolidated Hatch-Waxman cases. The plaintiff group of companies, AstraZeneca AB, Aktiebolaget Hässle, AstraZeneca LP, KBI Inc., and KBI-E Inc. (collectively, “AstraZeneca” or “plaintiff”),

has sued defendants Andrx Labs, LLC, Andrx Corporation, and Actavis, Inc. (collectively, "Andrx") in Civil Action No. 14-8030. Plaintiff has sued defendants Perrigo Company, PLC, Perrigo Company, L. Perrigo Company, and Paddock Laboratories, LLC (collectively, "Perrigo") in Civil Action No. 15-1057.

Both cases arise under 35 U.S.C. § 271(e)(2). AstraZeneca alleges in each case that a drug product that the named defendants propose to market infringes claims of U.S. Patent Nos. 6,369,085 ("the '085 Patent") and 7,411,070 ("the '070 Patent") (together, "the patents-in-suit").

The claim construction proceedings in both of these cases (and in a related case against Mylan Laboratories that recently settled, Civil Action No. 12-1378) were conducted jointly. This procedure was used because both cases involve the same two patents-in-suit, and the same three claim terms are disputed in each case. Nevertheless, each defendant group is a potential marketplace competitor and has its own claim construction positions, which we will address in the course of this opinion. Citations to the record of docketed filings in the body of this opinion will refer to Civil Action No. 14-8030. Citations to filings in the other two case dockets will be placed in the footnotes, for reasons explained here in the margin.[1]

[1] We begin with a procedural note. Due to the joint nature of these proceedings in two non-consolidated cases, this opinion is filed on the docket of each case. Those are, as stated, the case against Andrx ("the Andrx action"), Civil Action No. 14-8030; and the case against Perrigo ("the Perrigo action"), Civil Action No. 15-1057. There is a certain amount of overlap in the claim construction filings of the parties in each case, as would be expected, although of course there are also individual filings pertinent only to each respective case. The procedural picture is further complicated by the fact that filings in the now-settled Civil Action No. 12-1378, against Mylan ("the Mylan action"), were largely duplicative of filings in the other two cases as well.

AstraZeneca sells Nexium®, one of the drugs known as "proton pump inhibitors," or "PPIs," that are used in the treatment of disorders caused by stomach acid reflux. The FDA approved Nexium® in 2001. Although many of the patents that protected it are currently expired, the '085 and '070 Patents will not expire until May 25, 2018. (Dkt. 1 at 4-5.) The patents-in-suit claim the magnesium salt of S-omeprazole trihydrate, the form of the compound that AstraZeneca uses as the active pharmaceutical ingredient ("API") in Nexium®. (Id. at 4.)

Andrx has submitted to the FDA an Abbreviated New Drug Application ("ANDA") seeking approval for a generic version of Nexium®. (Id. at 7.) The Andrx ANDA includes "Paragraph IV certifications," asserting that the patents-in-suit are invalid, unenforceable, or will not be infringed by Andrx's ANDA product. (Id.) Separately and independently, Perrigo has submitted to the FDA an ANDA seeking

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All three groups of defendants participated and argued at the claim construction hearing, each defendant referring to the docket filings in its individual case.

This claim construction opinion thoroughly addresses the positions of all of the litigants in the two current cases, the Andrx action and the Perrigo action, with occasional reference to the now-settled Mylan action where relevant. However, in an effort to make clear and consistent the record citations here, the Court will use the following citation protocol.

All record citations in the body of the opinion are to the docket of the Andrx case, Civil Action No. 14-8030. Record citations to the Perrigo case, Civil Action No. 15-1057, are placed in the margin as footnotes, and designated "Perrigo action." Likewise, citations to the settled Mylan case, Civil Action No. 12-1378, are in the footnotes and designated "Mylan action."

Document entry numbers filed on the Electronic Case Filing System ("ECF") are cited as "dkt." Page pincites refer to the ECF pagination, e.g., "dkt. 46-1 at 33-35."

Thus, ECF citations in the body of the opinion are simply "dkt.," referring to the docket in the Andrx case, Civil Action No. 14-8030. ECF citations to the Andrx case in the footnotes also use the format "dkt." ECF citations to the Perrigo case and the Mylan case in the footnotes use the format, e.g., "Perrigo action, dkt. 52-1 at 12-15."

approval for its generic version of Nexium®, described as esomeprazole magnesium delayed-released capsules, 20 mg, including a Paragraph IV certification against the same two patents-in-suit.[2]

The '085 Patent, issued in 2002, is entitled "Form of S-Omeprazole."[3] The '070 Patent, based on a divisional application related to the '085 Patent, has the same name and was issued in 2008. The '070 Patent is subject to a terminal disclaimer whereby both patents will expire on May 25, 2018. (Dkt. 1 at 4-5.) All parties agree that the priority date for published prior art is May 30, 1997, based on a Swedish priority application date. (Dkt. 81.)

This opinion construes a claim term common to both patents-in-suit, a claim term in the '070 Patent, and a claim term in the '085 Patent. The primary issue concerns construction of the common claim term, which constitutes the entirety of claim 1 of the '070 Patent. It is "[t]he magnesium salt of S-omeprazole trihydrate." (See n. 10, infra.) The same claim term appears, with various limitation language, in all other claims of both patents. The Court has reviewed the written submissions of the parties, and conducted a two-day claim construction hearing based on those submissions and the oral arguments of the parties.

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[2] (Perrigo action, dkt. 1 at 5.)

[3] The '085 Patent is Exhibit A to the Complaint in both the Andrx action and the Perrigo action. (See, e.g., dkt. 1-2 at 2-14.) Likewise, the '070 Patent is Exhibit B to each Complaint. (See, e.g., dkt. 1-3 at 2-12.) Copies of both patents-in-suit are also attached as exhibits to various Markman papers filed in each case. We will simply cite those patents by page, drawing sheet, or column and line number.

The Court concludes, for the reasons stated herein, that an appropriate construction of the term "the magnesium salt of S-omeprazole trihydrate" is "the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole." The other two claim terms in dispute are also construed as explained in this opinion.

I. BACKGROUND

A. Procedural background

There is a long history of patent litigation relating to AstraZeneca's successful Nexium® products containing the active pharmaceutical ingredient omeprazole. We will not attempt to recount that history here in detail. Some aspects of that history, of which this Court and the parties are well aware, are pertinent to the present claim construction issues. Here is a brief summary of those aspects of the procedural background.

AstraZeneca's '085 and '070 Patents are part of one family of patents (including some that have expired) that have covered Nexium® products down through the years since initial FDA approval in 2001. Those patents include a patent issued as recently as 2013. We will refer to that patent family as the '085 Patent Family, and we have docketed a chart identifying that group of patents. (Dkt. 106.) The Nexium® product line has been the subject of numerous challenges by entities seeking FDA approval to sell generic versions in the U.S. market.[4]

[4] There is another pharmaceutical product line named Vivomo®, also formerly marketed by AstraZeneca and now marketed by a successor entity, that contains the same omeprazole API as used in Nexium® and has been covered also by the same group of patents, as well as other patents directed to those pharmaceutical compositions. The Vivomo® products are the subject

The litigation stemming from those generic challenges has been extensive in this Court, beginning in 2005 when the first Hatch-Waxman case pertaining to Nexium® was brought here.[5] That body of Nexium® litigation has also involved an earlier-established AstraZeneca patent family, also pertaining to omeprazole, that included now-expired U.S. Patent No. 5,714,504 (the "'504" Patent). We will refer to that patent family as the '504 Patent Family, and we have also docketed a chart identifying that group of patents. (Dkt. 105.) The first Hatch-Waxman case in this line, filed in 2005, for example, had as its patents-in-suit the '504 Patent, the '085 Patent, and another patent in the '504 Patent Family. See AstraZeneca AB, et al. v. Dr. Reddy's Laboratories, Ltd., et al., Civil Action No. 05-5553, dkt. 246, 2010 WL 1981790 (D.N.J. May 18, 2010).

Claim construction opinions have been rendered in some of these cases, pertaining to the claim terms at issue in this matter and other related claim terms in these two Patent Families. See Sections II.B.1.e and II.B.4, infra. While not binding on the parties in the current matter, those opinions are of record and cannot be overlooked by this Court in ruling on the issues presented here.

The landscape of Nexium® Hatch-Waxman litigation in this Court includes a long line of closed cases.[6] It also includes numerous more recent and currently-pending cases,

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of another group of Hatch-Waxman cases in this Court, not listed here. See, e.g., Horizon Pharma, Inc., et al. v. Dr. Reddy's Laboratories Inc., et al., Civil Action No. 11-2317.

[5] The Civil Action numbers for the original group of Nexium® cases in this Court, now all completed, were No. 05-5553, No. 06-1057, No. 08-328, and No. 08-4993. Those actions were against various defendants including Ranbaxy, Teva, and Dr. Reddy's Laboratories.

[6] As shown in n. 5, supra, the original Nexium®-related ANDA cases in this Court were filed between 2005 and 2008. This line of litigation has continued unabated since that time.

including the Andrx and Perrigo actions that are the subject of this opinion. In fact, new cases in this group continue to be filed.

A listing of the currently-pending Nexium® Hatch-Waxman cases in this Court is set forth in the margin.[7] The parties in several of those other cases have filed stipulations agreeing to be bound by the claim construction rulings rendered in this opinion, subject to any appellate review. See, e.g., Civil No. 14-4782, dkt. 59; Civil No. 15-6025, dkt. 56; and Civil No. 15-7415, dkt. 28.

B. The asserted '085 and '070 Patents and claims

The '085 Patent was filed on June 8, 1998, and was issued to AstraZeneca AB as assignee on April 9, 2002. ('085 Pat., pg. 1.) It is entitled "FORM OF S-OMEPRAZOLE." (Id.) Plaintiff states that the '085 Patent will expire on May 25, 2018, with pediatric exclusivity until November 25, 2018. (Dkt. 1 at 4.) The '085 Patent contains twelve claims and five drawing sheets. Claim 1 is independent. Claims 2-12 depend from claim 1, directly or indirectly. The claims of the '085 Patent are reproduced in the margin.[8]

Some of the more recently-closed cases include the following Civil Actions (listed by docket number and lead defendant name): No. 12-1378 (Mylan); No. 13-1669 (Actavis); No. 13-7298 (Aurobindo); No. 13-7299 (Kremers); No. 14-7263 (Actavis); No. 14-7870 (Actavis); No. 15-6609 (Alkem).

[7] The Civil Action numbers for the currently pending Nexium® ANDA cases here, in addition to the Andrx action and the Perrigo action captioned in this opinion (likewise listed by lead defendant name), are No. 13-4854 (Wockhardt); No. 14-4782 (Zydus); No. 15-6025 (Hec); No. 15-6092 (Lupin); No. 15-7415 (Zydus); No. 15-8267 (Dr. Reddy's); No. 16-1682 (Macleods); No. 16-2442 (Hetero); No. 16-4414 (Aurobindo); and 16-7330 (Glenmark).

[8] **Claim 1**. The magnesium salt of S-omeprazole trihydrate, wherein the compound is characterized by the following major peaks in its X-ray diffractogram:

d-value / Å	Relative Intensity
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s
8.3	w
16.6	vs

Claim 2. The magnesium salt of S-omeprazole trihydrate according to claim 1, wherein the compound is in a highly crystalline form.

Claim 3. The magnesium salt of S-omeprazole trihydrate according to claim 1, wherein the compound is in a stable form.

Claim 4. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to any of claims 1, 2 or 3 which comprises treating a magnesium salt of S-omeprazole of any other form with water.

Claim 5. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to any of claims 1, 2 or 3 which comprises the following steps:

a) mixing a potassium salt of S-omeprazole with an organic solvent;
b) converting the potassium salt of S-omeprazole into a corresponding magnesium salt of S-omeprazole by treating the potassium salt with a magnesium source;
c) precipitating the magnesium salt of S-omeprazole by addition of a non-solvent;
d) isolating the obtained magnesium salt of S-omeprazole;
e) treating the obtained magnesium salt of S-omeprazole with water, and
f) isolating and drying the obtained magnesium salt of S-omeprazole trihydrate.

Claim 6. The process according to claim 5, wherein the organic solvent of step a) is methanol.

Claim 7. The process according to claim 5, wherein the non-solvent of step c) is acetone.

Claim 8. The process according to claim 5 wherein steps a) to e) are replaced by the following single step: converting the potassium salt of S-omeprazole into a corresponding magnesium salt of S-omeprazole by treating the potassium salt with a magnesium source in water.

Claim 9. The process according to claim 5, wherein the magnesium source is magnesium sulfate.

Claim 10. The process according to claim 8, wherein the magnesium source is magnesium sulfate.

With respect to Andrx, AstraZeneca asserts infringement of claims 1-4 and 12 of the '085 Patent. (Dkt. 38 at 5-6.) With respect to Perrigo, AstraZeneca asserts infringement of at least claims 1-4 and 11-12 of the '085 Patent.[9]

The '070 Patent, also entitled "FORM OF S-OMEPRAZOLE," was filed on September 25, 2003, and was issued to plaintiff AstraZeneca AB as assignee on August 12, 2008. ('070 Pat., p.1.) The '070 Patent was terminally disclaimed over the '085 Patent, making its expiration date the same as that of the '085 Patent. (See Id.) The '070 Patent contains four claims and five drawing sheets. Claim 1 is independent. Claims 2-4 depend from claim 1, directly or indirectly. The claims of the '070 Patent are reproduced in the margin.[10]

Claim 11. A pharmaceutical composition comprising the magnesium salt of S-omeprazole trihydrate according to any of claims 1, 2 or 3 as active ingredient and a pharmaceutically acceptable carrier.

Claim 12. A method of treating a gastric acid related condition which method comprises administering to a subject suffering from said condition a therapeutically effective amount of the magnesium salt of S-omeprazole trihydrate according to any of claims 1, 2 or 3. ('085 Pat., col. 10, l. 15 – col. 12, l. 5.)

[9] (Perrigo action, dkt. 44 at 7.)

[10] **Claim 1**. The magnesium salt of S-omeprazole trihydrate.

Claim 2. The magnesium salt of S-omeprazole trihydrate according to claim 1 represented by FIG. 1.

Claim 3. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim 1 which comprises treating a magnesium salt of S-omeprazole of any other form with water.

Claim 4. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim 2 which comprises treating a magnesium salt of S-omeprazole of any other form with water. ('070 Pat., col. 10, ll. 51-62.)

AstraZeneca asserts infringement of claims 1-4 of the '070 Patent against both Andrx and Perrigo. (See dkt. 38 at 5-6.)[11]

The '085 and '070 Patents are two of several patents originating from an international application filed May 25, 1998, including United States Patents No. 6,747,155, No. 6,677,455, No. 7,745,466, No. 8,076,361, and No. 8,466,175. (See dkt. 106.) All of the above-listed patents are directed to various forms of S-omeprazole and methods, processes, or compositions employing those forms. They all share essentially the same specification language.

Omeprazole is the generic name for the compound 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole. ('070 Pat., col. 1, ll. 25-27.) It is a proton pump inhibitor and is useful as an antiulcer agent. (Id., col. 1, ll. 29-31.) It is a sulfoxide and chiral compound with the sulfur atom being the stereogenic center, meaning omeprazole is a racemic mixture of its two single enantiomers, the R- and S-enantiomers of omeprazole. (Id., col. 1, ll. 35-38.) The Background section of the '070 Patent acknowledges that certain salts of single enantiomers of omeprazole, including magnesium salts of R- and S-omeprazole, were previously disclosed in the prior art. (Id., col. 1, ll. 25-58.)

The Field of Invention and Abstract sections of the '085 and '070 Patents, which are nearly identical, state that the invention relates to a novel form of S-omeprazole, and more specifically to a novel form of the magnesium salt of the S-enantiomer of

[11] (See Perrigo action, dkt. 44 at 7.)

omeprazole trihydrate. (Id., col. 1, ll. 12-17.) These sections also state that the invention relates to processes for preparing such a novel form and the pharmaceutical compositions containing it, as well as intermediates used in the process, and their preparation. (Id., col. 1, ll. 17-21.) The claim construction dispute in this action centers upon the magnesium salt of the S-enantiomer of omeprazole trihydrate.

C. Disputed claim terms

The parties have identified four claim terms requiring construction in this matter: (1) "highly crystalline form;" (2) "the magnesium salt of S-omeprazole trihydrate;" (3) "characterized by the following major peaks in its X-ray diffractogram;" and (4) represented by FIG. 1." (See dkt. 36 at 2-3.)[12] As discussed in more detail below, three of these four claim terms are disputed by the parties.

1. "highly crystalline form"

The claim term "highly crystalline form" appears only in dependent claim 2 of the '085 Patent. See n. 8, supra. However, that term is incorporated by reference into dependent claims 4-12 of the '085 Patent. See id. Claims 1 and 2 of the '085 Patent state as follows:

> 1. The magnesium salt of S-omeprazole trihydrate, wherein the compound is characterized by the following major peaks in its X-ray diffractogram:

[12] (See Perrigo action, dkt. 37 at 2-3.)

d-value / Å	Relative Intensity
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s
8.3	w
16.6	vs

2. The magnesium salt of S-omeprazole trihydrate according to claim 1, wherein the compound is in a **highly crystalline form**.

('085 Pat., col. 10, ll. 15-37 (emphasis added).)

For the purposes of this case, the parties agree that this term means "having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art." (Dkt. 36 at 2.)[13]

2. "the magnesium salt of S-omeprazole trihydrate"

The term "the magnesium salt of S-omeprazole trihydrate" is applicable to claims 1-12 of the '085 Patent and claims 1-4 of the '070 Patent. The term appears in claims 1-5 and 11-12 of the '085 Patent and claims 1-4 of the '070 Patent. See nn. 8, 10, supra. Independent claim 1 of the '085 Patent, in which the term first appears, is reproduced above in Section I.C.1. The term is incorporated by reference into dependent claims 6-10 of the '085 Patent. See n. 8, supra. Claim 1 of the '070 Patent, in which the term first

[13] (Perrigo action, dkt. 37 at 2.)

appears, states in its entirety: "The magnesium salt of S-omeprazole trihydrate." ('070 Pat., col. 10, l. 52.) The parties' respective constructions are as follows:

Term Identified for Construction	AstraZeneca's Proposed Construction	Andrx's Proposed Construction	Perrigo's Proposed Construction
the magnesium salt of S-omeprazole trihydrate	a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-omeprazole	the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole	crystals of the magnesium salt of S-omeprazole trihydrate, substantially free from magnesium salts of R-omeprazole and other forms of magnesium salts of S-omeprazole

(See dkt. 36 at 3.)[14,15]

AstraZeneca's proposed construction of this term is identical to the construction Judge Pisano arrived at in AstraZeneca AB v. Dr. Reddy's Laboratories Inc., No. 11-2317 (JAP), 2013 WL 1847639 (D.N.J. May 1, 2013). In that case, AstraZeneca offered the following construction: the "magnesium salt of S-omeprazole having approximately three molecules of bound water per molecule of S-omeprazole magnesium." Id. at *8.[16]

[14] (Perrigo action, dkt. 37 at 3.)

[15] Mylan's proposed construction for this term was similar to Andrx's proposed construction and was "the substantially pure crystalline magnesium salt of S-omeprazole having exactly three waters of hydration." (Mylan action, dkt. 218 at 2.)

[16] The construction offered by AstraZeneca was submitted shortly before the Markman hearing in that case, and differed from a prior proposed construction offered by AstraZeneca. See AstraZeneca AB v. Dr. Reddy's Laboratories Inc., No. 11-2317 (JAP), 2013 WL 1847639 at n.1 (D.N.J. May 1, 2013). AstraZeneca's initial construction for the term broke the term into two separate parts: "magnesium salt of" and "S-omeprazole trihydrate." For "magnesium salt of," AstraZeneca proposed the following meaning: "a compound formed between positively-charged

The defendants, in that case, proposed this construction: "a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-omeprazole in a unit cell of the crystal lattice that is substantially free from magnesium salts of R-omeprazole and other prior art forms of magnesium salts of S-omeprazole including S-omeprazole dihydrate and amorphous forms." Id. Relying on a comparison of the claims, the court found that the term was "intended to have a broad construction" and refused to import the limitations sought by defendants. Id. However, the court did not adopt AstraZeneca's proposed construction either, noting AstraZeneca's proposal was flawed in that it sought to define the trihydrate as having "approximately" three molecules of water, a definition that ran afoul of the plain and ordinary meaning of the term "trihydrate." Id. Thus, the court construed the term to mean "a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-omeprazole." Id.

3. "characterized by the following major peaks in its X-ray diffractogram"

The term "characterized by the following major peaks in its X-ray diffractogram" appears only in claim 1 of the '085 Patent, which is reproduced above in Section I.C.1.

Magnesium (Mg) cations and negatively-charged esomeprazole anions." AstraZeneca AB v. Dr. Reddy's Laboratories Inc., No. 11-2317, dkt. 50-1 at 4. For "S-omeprazole trihydrate," AstraZeneca proposed the following meaning: "(S)-omeprazole having a structure that has a theoretical ratio of three molecules of bound water per molecule of $((S)\text{-omeprazole})_2$ magnesium, but which does not necessarily contain exactly three molecules of water, whose structure may be determined by analytical methods identified in the patent and known to those of ordinary skill. In the '085 patent the structure is determined by examining XRD." Id. at 4-5.

The term is incorporated by reference into dependent claims 2-12 of the '085 Patent. See n. 8, supra. The parties' respective constructions are as follows:

Term Identified for Construction	AstraZeneca's Proposed Construction	Andrx's Proposed Construction	Perrigo's Proposed Construction
characterized by the following major peaks in its X-ray diffractogram	identifiable by reference to an X-ray diffractogram that includes the major peaks below	exhibiting, within the range of normal experimental error, each of the following as major peaks in its X-ray diffractogram, each such peak falling within the range for relative intensity recited for the peak, such ranges being defined at Column 5, lines 28-39	having each of the referenced major peaks in its X-ray powder diffractogram within normal experimental error

(Dkt. 36 at 3.)[17,18] The relative intensity range definitions provided at column 5, lines 28-39 of the '085 Patent, as referenced in Andrx' proposed construction, appear as follows:

% Relative Intensity	Definition
25–100	vs (very strong)
10–25	s (strong)
3–10	m (medium)
1–3	w (weak)
<1	vw (very weak)

('085 Pat., col. 5, ll. 32-39.)

[17] (Perrigo action, dkt. 37 at 3.)

[18] Mylan's proposed construction for this term was similar to Perrigo's proposed construction and was "the magnesium salt of the S-omeprazole trihydrate has an x-ray diffraction diffractogram having each peak as set forth in the table in claim 1 within normal experimental error." (Mylan action, dkt. 218 at 2.)

AstraZeneca's proposed construction of this term is identical to the construction AstraZeneca proposed in AstraZeneca AB v. Dr. Reddy's Laboratories Inc., which was adopted verbatim by that court. The defendants' proposed construction for the term was "having all of the referenced major peaks in its X-ray diffractogram," a construction similar to that proposed by both Andrx and Perrigo in this matter. See AstraZeneca AB, No. 11-2317, 2013 WL 1847639 at *8-9. In adopting AstraZeneca's proposed construction, the Court found that the defendants' proposed construction was too rigid and that it failed to account for experimental error:

> The Court concludes that Defendants' construction, which would require an exact match, is too rigid. The claim language requires only that the S-omeprazole trihydrate be "characterized" by the peaks in the table, not necessarily that it have a perfect one-to-one relationship. Even Defendants' expert concedes that although the X-ray diffraction of a compound will have the same "general appearance," the positions of the peaks may differ somewhat because of slight experimental errors. Plaintiffs' construction accounts for such differences, while Defendants' would not.

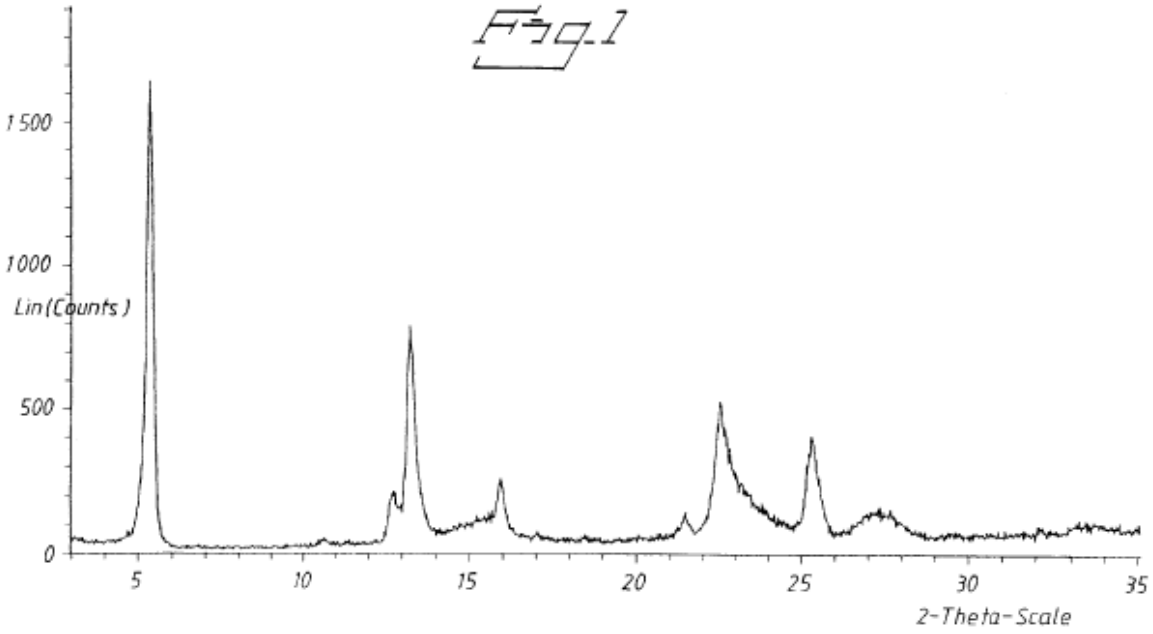
Id. at *9.

4. "represented by FIG. 1"

The term "represented by FIG. 1" appears only in claim 2 of the '070 Patent. Claim 2 of the '070 Patent states: "The magnesium salt of S-omeprazole trihydrate according to claim 1 represented by FIG. 1." ('070 Pat., col. 10, ll. 53-54.) The term is incorporated by reference into dependent claim 4 of the '070 Patent. See n. 10, supra. The parties' respective constructions are as follows:

Term Identified for Construction	AstraZeneca's Proposed Construction	Andrx's Proposed Construction	Perrigo's Proposed Construction
represented by FIG. 1	represented by Figure 1 of the '070 patent	exhibiting an x-ray powder diffractogram that is the same as Figure 1 of the '070 patent, within normal experimental error	having an X-ray powder diffractogram that is the same as Figure 1 of the '070 patent within normal experimental error

(Dkt. 36 at 3.)[19,20] Figure 1 of the '070 Patent, which is described as an "X-ray powder diffractogram of the magnesium salt of S-omeprazole trihydrate prepared according to the present invention," ('070 Pat., col. 1, ll. 62-64), is reproduced below:



[19] (Perrigo action, dkt. 37 at 3.)

[20] Mylan's proposed construction for this term was identical to Andrx's proposed construction. (See Mylan action, dkt. 218 at 2.)

('070 Pat., Fig. 1.) Figure 1 of the '070 Patent is identical to Figure 1 of the '085 Patent. (Compare '070 Pat., Fig. 1 with '085 Pat., Fig. 1.) The written description explains that the data in Example 1, Table 1 is a reading of the X-ray powder diffractogram depicted in Figure 1. (See '070 Pat., col. 5, ll. 26 – col. 6, ll. 10.)

AstraZeneca's proposed construction of this term is identical to the construction AstraZeneca proposed in AstraZeneca AB v. Dr. Reddy's Laboratories Inc., which was adopted verbatim by that court. The defendants' proposed construction for the term was "having an X-ray diffractogram the same as FIG. 1," a construction similar to that proposed by both Andrx and Perrigo. See AstraZeneca AB, No. 11-2317, 2013 WL 1847639 at *9. The court found the defendants' proposed construction to be too rigid for the same reasons it expressed with respect to defendants' proposed construction for the term "characterized by the following major peaks in its X-ray diffractogram." See id.

The written submissions of the parties on these claim construction issues are described in the margin.[21] In addition, the Court conducted a Markman hearing. (Dkt. 82, Markman Hr'g Tr. Vol. I; dkt. 83, Markman Hr'g Tr. Vol. II.)

[21] In the Andrx action: dkt. 36 to dkt. 36-3, Joint Claim Construction & Prehearing Statement; dkt. 38, Andrx's Opening Br.; dkt. 38-1 to dkt. 38-2, Edwards I Decl.; dkt. 38-3, Zaworotko I Decl.; dkt. 39, Plaintiff's Opening Br.; dkt. 39-1 to dkt. 39-10, Stole I Decl.; dkt. 40 to dkt. 40-17, Byrn I Decl.; dkt. 50, Andrx's Responsive Br.; dkt. 47-1, Edwards II Decl.; dkt. 47-2, Zaworotko II Decl.; dkt. 48, Plaintiff's Responsive Br.; dkt. 48-1 to dkt. 48-16, Stole II Decl.; dkt. 49 to dkt. 49-8, Byrn II Decl.; dkt. 54, Andrx's Reply Br.; dkt. 54-1, Zaworotko III Decl.; dkt 80 to dkt. 80-3, Plaintiff's Ltr. 5/24/16 with attachments; dkt. 86-1, Gannon Decl. with exhibits. Plaintiff also submitted supplemental materials under seal, pertaining to the Andrx ANDA product. (Dkt. 77, dkt. 77-1, dkt. 84 to dkt. 84-3, all SEALED.) Andrx objected to these materials as irrelevant to the pending Markman proceedings. (Dkt. 89.) The Court agrees with Andrx on this point. Nevertheless, we have reviewed those sealed submissions from plaintiff, and we do not find that the contents would change the claim construction rulings set forth here.

II. DISCUSSION

A. Legal standard

"It is a 'bedrock principle' of patent law that 'the claims of a patent define the invention to which the patentee is entitled the right to exclude.'" Phillips v. AWH Corp., 415 F.3d 1303, 1312 (Fed. Cir. 2005) (en banc) (quoting Innova/Pure Water Inc. v. Safari Water Filtration Sys., Inc., 381 F.3d 1111, 1115 (Fed. Cir. 2004)). Claim construction determines the correct claim scope, and is a determination exclusively for the court as a matter of law. Markman v. Westview Instruments, Inc., 52 F.3d 967, 978-79 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996). The focus in construing disputed terms in claim language "is on the objective test of what one of ordinary skill in the art at the time of the invention would have understood the term[s] to mean." Id. at 986.

In the Perrigo action: Perrigo action, dkt. 37 to dkt. 37-3, Joint Claim Construction and Prehearing Statement; Perrigo action, dkt. 44, Perrigo's Opening Br.; Perrigo action, dkt. 44-1 to dkt. 44-2, Buckton I Decl.; Perrigo action, dkt. 44-3 to dkt. 44-22, Shrestha I Decl.; Perrigo action, dkt. 45, Plaintiff's Opening Br.; Perrigo action, dkt. 45-1 to dkt. 45-10, Stole I Decl.; Perrigo action, dkt. 46 to dkt. 46-17, Byrn I Decl.; Perrigo action, dkt. 50, Perrigo's Responsive Br.; Perrigo action, dkt. 50-1, Buckton II Decl.; Perrigo action, dkt. 50-2 to dkt. 50-5, Shrestha II Decl.; Perrigo action, dkt. 51, Plaintiff's Responsive Br.; Perrigo action, dkt. 51-1 to dkt. 51-16, Stole II Decl.; Perrigo action, dkt. 52 to dkt. 52-8, Byrn II Decl.; Perrigo action, dkt. 70, Perrigo Ltr. 5/6/16; Perrigo action, dkt. 72 to dkt. 72-1, Flax Decl.; Perrigo action, dkt 76 to dkt. 76-3, Plaintiff's Ltr. 5/24/16 with attachments; Perrigo action, dkt. 83, Perrigo Joint Reply Ltr. 6/13/16.

In the Mylan action: Mylan action, dkt. 218 to 218-2, Joint Claim Construction and Prehearing Statement; Mylan action, dkt. 230, Plaintiff's Opening Br.; Mylan action, dkt. 230-1 to dkt. 230-10, Stole I Decl.; Mylan action, dkt. 231 to dkt. 231-17, Byrn I Decl.; Mylan action, dkt. 232, Mylan's Opening Br.; Mylan action, dkt. 232-1 to dkt. 232-15, Beel I Decl.; Mylan action, dkt. 232-16 to dkt. 232-17, Atwood I Decl.; Mylan action, dkt. 232-18 to dkt. 232-19, Ruffolo Decl.; Mylan action, dkt. 244 to dkt. 244-1, Mylan's Responsive Br.; Mylan action, dkt. 245, Plaintiff's Responsive Br.; Mylan action, 245-1 to 245-16, Stole II Decl., Mylan action, dkt. 246 to dkt. 246-8, Byrn II Decl.; Mylan action, dkt. 247 to 247-5, Beel II Decl.; Mylan action, dkt. 247-6, Atwood II Decl.; Mylan action, dkt. 247-7, Ruffolo II Decl.; Mylan action, dkt. 269, Mylan's Reply Br.; Mylan action, dkt. 269-1 to dkt. 269-2, Atwood III Decl.

To determine the meaning of the claims, courts start by considering the intrinsic evidence. Phillips, 415 F.3d at 1313; C.R. Bard, Inc. v. U.S. Surgical Corp., 388 F.3d 858, 861 (Fed. Cir. 2004); Bell Atl. Network Servs., Inc. v. Covad Commc'ns Group, Inc., 262 F.3d 1258, 1267 (Fed. Cir. 2001). The intrinsic evidence includes the claims themselves, the specification, and the prosecution history. Phillips, 415 F.3d at 1314; C.R. Bard, Inc., 388 F.3d at 861.

The claims themselves provide substantial guidance in determining the meaning of particular claim terms. Phillips, 415 F.3d at 1314. First, the context in which a term is used in the asserted claim can be very instructive. Id. Other asserted or unasserted claims can aid in determining the claim's meaning because claim terms are normally used consistently throughout a patent. Id. Differences among claims can also assist in understanding a term's meaning. Id. For example, when a dependent claim adds a limitation, there is a presumption that the independent claim does not include that limitation. Id. at 1314-15.

"[C]laims 'must be read in view of the specification of which they are a part.'" Id. at 1315 (quoting Markman, 52 F.3d at 979). "[T]he specification 'is always highly relevant to the claim construction analysis. Usually, it is dispositive; it is the single best guide to the meaning of a disputed term.'" Id. (quoting Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996)). This is true because a patentee may define his own terms, give a claim term a different meaning than the term would otherwise possess, or disclaim or disavow the claim scope. Id. at 1316. In these circumstances, the inventor's lexicography governs. Id. The specification may also resolve the meaning of

ambiguous claim terms "where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1325 (Fed. Cir. 2002). But, "[a]lthough the specification may aid the court in interpreting the meaning of disputed claim language, particular embodiments and examples appearing in the specification will not generally be read into the claims." Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed. Cir. 1998) (quoting Constant v. Advanced Micro-Devices, Inc., 848 F.2d 1560, 1571 (Fed. Cir. 1988)); accord Phillips, 415 F.3d at 1323.

The prosecution history is another tool to supply the proper context for claim construction. It "can often inform the meaning of the claim language by demonstrating how the inventor understood the invention and whether the inventor limited the invention in the course of prosecution, making the claim scope narrower that it would otherwise be." Phillips, 415 F.3d at 1317.

"Extrinsic evidence consists of all evidence external to the patent and prosecution history, including expert and inventor testimony, dictionaries, and learned treatises." Markman, 52 F.3d at 980. Although extrinsic evidence can be useful, it is "less significant than the intrinsic record in determining 'the legally operative meaning of claim language.'" Phillips, 415 F.3d at 1317 (quoting C.R. Bard, Inc., 388 F.3d at 862).

Dictionaries and treatises may aid a court in understanding the underlying technology and the manner in which one skilled in the art might use claim terms, but dictionaries and treatises may provide definitions that are too broad or may not be

indicative of how the term is used in the patent. Id. at 1318. Similarly, expert testimony may aid a court in understanding the underlying technology and determining the particular meaning of a term in the pertinent field, but an expert's conclusory, unsupported assertions as to a term's definition are entirely unhelpful to a court. Id.

Generally, extrinsic evidence is "less reliable than the patent and its prosecution history in determining how to read claim terms." Id. The Supreme Court recently explained the role of extrinsic evidence in claim construction:

> In some cases, however, the district court will need to look beyond the patent's intrinsic evidence and to consult extrinsic evidence in order to understand, for example, the background science or the meaning of a term in the relevant art during the relevant time period. See, e.g., Seymour v. Osborne, 11 Wall. 516, 546, 20 L.Ed. 33 (1871) (a patent may be "so interspersed with technical terms and terms of art that the testimony of scientific witnesses is indispensable to a correct understanding of its meaning"). In cases where those subsidiary facts are in dispute, courts will need to make subsidiary factual findings about that extrinsic evidence. These are the "evidentiary underpinnings" of claim construction that we discussed in Markman, and this subsidiary factfinding must be reviewed for clear error on appeal.

Teva Pharm. USA, Inc. v. Sandoz, Inc., 135 S. Ct. 831, 841 (2015).

As is sometimes the case, the claim terms requiring construction may have been the subject of prior claim construction proceedings by other district courts, or even the same court. While rulings of the Federal Circuit on issues of claim construction for a given patent are binding on later district courts analyzing the same patent, interpretations of the same or other district courts of the same terms in the patent or patent family are generally not binding. See Shire Dev. LLC v. Amneal Pharms. LLC, No. 15-2865, 2016

WL 4119940, at *2 (D.N.J. Aug. 2, 2016); see also Ravo v. Tyco Healthcare Group LP, No. 11-1637, 2013 WL 3326657, at *6 (W.D. Pa. Mar. 13, 2013). However, the interpretations of the same or other district courts are generally considered to be highly relevant and persuasive authority. Id.

Overall, in construing the claims, "[t]he judge's task is not to decide which of the adversaries is correct. Instead, the judge must independently assess the claims, the specification, and if necessary the prosecution history and relevant extrinsic evidence, and declare the meaning of the claims." Exxon Chem. Patents, Inc. v. Lubrizol Corp., 64 F.3d 1553, 1556 (Fed. Cir. 1995).

B. Application

1. Summary of intrinsic evidence

In this section, we will summarize the intrinsic evidence of record, *i.e.*, the language of the claims, the common written description, and the prosecution history of the '085 and '070 Patents.

a. Relevant claim terms

As discussed above in Section I.C, supra, both of the disputed claim terms of the '085 Patent appear for the first time in independent claim 1. Claim 1 of the '085 Patent, with the disputed claim terms highlighted, states:

> **Claim 1**. **The magnesium salt of S-omeprazole trihydrate**, wherein the compound is **characterized by the following major peaks in its X-ray diffractogram**:

d-value / Å	Relative Intensity
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s
8.3	w
16.6	vs

('085 Pat., col. 10, ll. 15-34.) AstraZeneca admits that claim 1 of the '085 Patent is limited to a specific form of the magnesium salt of S-omeprazole magnesium characterized by certain X-ray diffraction "d-values," which are indicative of crystalline material. (Dkt. 39 at 8-9.) Dependent claims 2-12 recite either further limitations to claim 1, a process for preparing the claimed product, a pharmaceutical composition comprising the claimed product, or a method for treating a gastric acid related condition with the claimed product. ('085 Pat., col. 10, l. 2 – col. 12, l. 6.)[22] The claim term "characterized by the following major peaks in its X-ray diffractogram" appears only in claim 1 of the '085 Patent.

As discussed above in Section I.C, supra, both of the disputed claim terms of the '070 Patent appear for the first time in claims 1 and 2. Claims 1 and 2 of the '070 Patent, with the disputed claim terms highlighted, state:

Claim 1. **The magnesium salt of S-omeprazole trihydrate**.

[22] As discussed above, claims 2-5, and 11-12 of the '085 Patent also include the claim term "the magnesium salt of S-omeprazole trihydrate." See n. 8, supra.

> **Claim 2**. **The magnesium salt of S-omeprazole trihydrate** according to claim 1 **represented by FIG. 1**.

('070 Pat., col. 10, ll. 51-54.) Dependent claims 3 and 4 each describe a process for preparing the magnesium salt of S-omeprazole trihydrate. (See '070 Pat., col. 10, ll. 55-62.)[23] The claim term "represented by FIG. 1" appears only in claim 2 of the '070 Patent. Claim 4 depends from claim 2, and incorporates the disputed term "represented by FIG.1."

The claim term "the magnesium salt of S-omeprazole trihydrate" appears in each of the relevant claims of both the '085 and '070 Patents; but it stands alone in claim 1 of the '070 Patent without further limitation. This is where most of the disagreement between the parties lies. AstraZeneca argues that, under the principles of claim differentiation, the later-issued claim 1 of the '070 Patent was issued without any restrictions as to form, and thus should not be limited to a crystalline form – as claim 1 of the '085 Patent admittedly is. (See dkt. 39 at 8-10.) Andrx and Perrigo both argue that claim differentiation does not require such a result because claim 1 of the '070 Patent can be broader than its dependent claim 2 and even claim 1 of the '085 Patent, while still being limited to a crystalline form. (See dkt. 38 at 18-19.)[24]

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[23] Claims 3 and 4 also include the claim term "the magnesium salt of S-omeprazole trihydrate." See n. 10, supra.

[24] (See Perrigo action, dkt. 50 at 22-23.)

b. Common '085 and '070 Patent written description

The '085 and '070 Patents share a common written description.[25] The written description varies only in the description of related applications. (Compare '085 Pat., col. 1, ll. 3-4, with '070 Pat., col. 1, ll. 3-8.) The patent figures of the '085 and '070 Patents, which are referenced in the written description, are identical.

In the Background section, the written description begins by describing the state of the art at the time of the invention. The inventors acknowledge that omeprazole and therapeutically acceptable salts thereof, including specific alkaline salts, have been disclosed in the prior art. ('070 Pat., col. 1, ll. 25-34.) The inventors also acknowledge that the (+)-enantiomer of the magnesium salt of omeprazole and (-)-enantiomer of the magnesium salt of omeprazole were known, and found to have an R and S configuration, respectively. (Id., col. 1, ll. 35-49.) Certain salts of single enantiomers of omeprazole (i.e., salts of S-omeprazole and R-omeprazole) were also known to have "improved pharmacokinetic and metabolic properties" that provide an "improved therapeutic profile such as a lower degree of interindividual variation." (Id., col. 1, ll. 50-54.) Processes for the preparation of single enantiomers of omeprazole and certain salts of single enantiomers of omeprazole were also known in the prior art, as were suitable tablet dosage forms of magnesium salts of the single enantiomers of omeprazole. (Id., col. 1, ll. 55-58.)

[25] When describing the contents of the common written description, we cite only the written description of the '070 Patent for convenience. We may also refer to the common written description as only "the written description" for convenience.

The inventors describe their invention as a novel form of S-omeprazole, specifically "a novel form of the magnesium salt of the S-enantiomer of omeprazole trihydrate." (Id., col. 1, ll. 11-16.) Their invention also includes processes for preparing the novel form as well as pharmaceutical compositions containing it. (Id., col. 1, ll. 16-18.)

The portions of the written description that the parties and their respective experts argue shape the construction of the claim terms appear in column two of the '070 Patent, and are quoted here in full:

> It has surprisingly been found that the magnesium salt of S-omeprazole occurs in a number of structurally different forms. It is an object of the present invention to provide a substantially pure magnesium salt of S-omeprazole trihydrate, hereinafter referred to as the compound of the invention. This trihydrate can be obtained as a well defined compound. The present invention also provides a process to obtain and a method of differentiating the magnesium salt of S-omeprazole trihydrate from other forms of magnesium salts of S-omeprazole.
>
> The compound of the invention is advantageous because it is more stable than the corresponding magnesium salt compounds in prior art and is therefore easier to handle and store. The compound of the invention is also easier to characterize because it exists in a well defined state. Additionally, the compound of the invention is easier to synthesize in a reproducible manner and thereby easier to handle in a full scale production.
>
> The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is substantially free from magnesium salts of R-omeprazole. The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is also substantially free from other forms of magnesium salts of S-omeprazole, such as the corresponding magnesium salt compounds described in prior art, and

> dihydrates used in the preparation of the trihydrate compound according to the present invention.
>
> The compound of the invention is characterized by the positions and intensities of the major peaks in the X-ray powder diffractogram, but may also be characterized by conventional FT-IR spectroscopy. These characteristics are not exhibited by any other form of magnesium salt of S-omeprazole and accordingly, the magnesium salt of S-omeprazole trihydrate is easily distinguishable from any other crystal form of the magnesium salt of S-omeprazole disclosed in prior art. The compound of the invention is characterized by being highly crystalline, i.e. having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art. With the expression "any other form" is meant anhydrates, hydrates, solvates, and polymorphs or amorphous forms thereof disclosed in the prior art. Examples of any other forms of magnesium salt of S-omeprazole includes [sic], but are not limited to, anhydrates, monohydrates, dihydrates, sesquihydrates, trihydrates, alcoholates, such as methanolates and ethanolates, and polymorphs or amorphous forms thereof.
>
> The compound of the invention may also be characterized by its unit cell.

('070 Pat., col. 2, ll. 15-64.) Generally, plaintiff argues that these paragraphs describe examples and embodiments and are not intended to limit the scope of the claims of either patent. Defendants, on the other hand, view some of these statements as describing the claimed invention, and argue they are thus limiting.

The parties also repeatedly refer to the following language found at column 3, lines 54-60:

> The compound of the invention, i.e. the magnesium salt of S-omeprazole trihydrate, prepared according to the present invention may be analyzed by XRPD, a technique which is known per se. The amount of water in the magnesium salt of S-omeprazole trihydrate is determined by thermogravimetric analysis, a technique which is known per se.

('070 Pat., col. 3, ll. 54-60.)

The written description provides multiple examples that "illustrate the preparation of the compound of the invention, according to different process routes and including new intermediates." (See '070 Pat., col. 5, l. 7 – col. 10, l. 50.) Examples 1, 4 and 7 are most relevant here.[26] The portion of the written description that pertains to Example 1 is reproduced below:

Example 1

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Trihydrate

> Water (157 kg) was added to the wet crystals of the magnesium salt of S-omeprazole, prepared according to Example 4, below. The mixture was heated to 38° C. with stirring and left for 3 hours. The crystals were filtered off and dried in vacuo. Yield: 31.6 kg.
>
> X-ray powder diffraction analysis was performed on a sample of the crystals prepared above according to standard methods, which can be found in e.g. Kitaigorodsky, A. I. (1973), Molecular Crystals and Molecules, Academic Press, New York; Bunn, C. W. (1948), Chemical Crystallography, Clarendon Press, London; or Klug, H. P. & Alexander, L. E. (1974), X-Ray Diffraction Procedures, John Wiley and Sons, New York. The analysis gave the diffractogram depicted in FIG. **1**. The main peaks, with positions and relative intensities, have been extracted from the diffractogram in FIG. **1** and is given below in table **1**. The relative intensities are less reliable

[26] The additional examples are directed to processes for the preparation of other compounds, (see '070 Pat., col. 6, l. 11 – col. 7, l. 18; col. 7, l. 33 – col. 9, l. 27), however those additional compounds need not be discussed in depth here. The additional compounds described are: the potassium salt of S-omeprazole (examples 2 and 3), and the magnesium salt of S-omeprazole dihydrate (examples 5 and 6).

and instead of numerical values the following definitions are used.

% Relative Intensity	Definition
25-100	vs (very strong)
10-25	s (strong)
3-10	m (medium)
1-3	w (weak)
<1	vw (very weak)

Some additional very weak peaks found in the diffractogram have been omitted from table **1**.

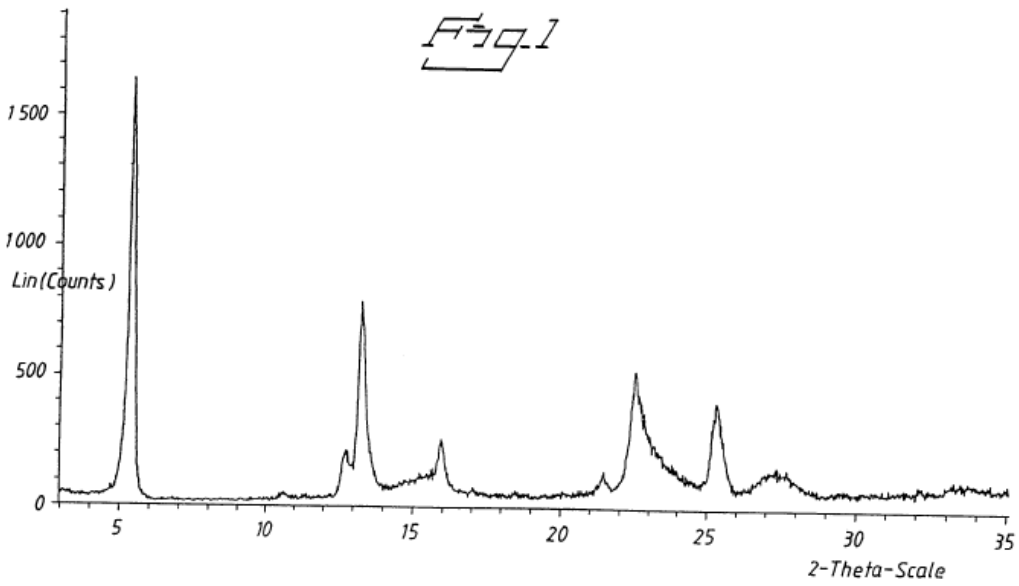
TABLE 1

Positions and intensities of the major peaks in the XRP-diffractogram of the magnesium salt of S-omeprazole trihydrate.

d-value / Å	Relative Intensity
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s
8.3	w
16.6	vs

('070 Pat., col. 5, l. 15 – col. 6, l. 10.)

As noted above, an X-ray powder diffraction analysis was performed on a sample of the crystals prepared according to Example 1. ('070 Pat., col. 5, ll. 26-33.) The written description explains that this X-ray powder diffraction analysis "gave the diffractogram depicted in FIG. 1 [reproduced below]." ('070 Pat., col. 5, ll. 33-34.)



('070 Pat., Fig. 1.)

During the Markman hearing, the parties explained that Figure 1 and Table 1 depicted the same test data, even though each of the 13 peaks set forth in Table 1 are not visible to the naked eye in Figure 1. (Dkt. 82 at 95-97.)

The product yielded by Example 7 was also analyzed using X-ray powder diffraction. ('070 Pat., col. 9, ll. 48-50.) The written description indicates that the X-ray powder diffraction result for this example "complies with FIG. 1 and Table 1." ('070 Pat., col. 9, ll. 48-50.) However, there is no further elaboration in the written description regarding the language "complies with." The portion of the written description that pertains to Example 7 is reproduced below:

Example 7

S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole Magnesium Salt Trihydrate

22.0 g (29,1 mmol) of S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl]sulfinyl]-1H-benzimidazole potassium salt was dissolved in 40 mL of water. The solution was seeded with 0.11 g (0,1 mmol) S-5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1H-benzimidazole magnesium salt trihydrate. 22 mL (69,6 mmol) of $MgSO_4$ (aq) was added under a 3 h period. The slurry was filtered off and the precipitate was elutriated in water for approximately 30 minutes and the crystals were filtered off and dried (35° C., vacuum).

Yield: 9.15 g (11,6 mmol; 80%). The substance had a purity (HPLC): 99.8 area %, Mg content: 3.40% (w/w) and ee: 99.8%.

The product was analyzed using X-ray powder diffraction and the result complies with FIG. 1 and Table 1.

('070 Pat., col. 9, ll. 30-50.)

Example 4 teaches a process for the preparation of the magnesium salt of S-omeprazole. (See '070 Pat., col. 7, ll. 19-32.) Example 1 notes that the magnesium salt of S-omeprazole prepared according to Example 4 is used as a precursor in Example 1. (Id. at col. 5, ll. 13-15.)

The written description concludes with a description of a prior art method of preparing a single enantiomer of omeprazole magnesium salt, identified as "Reference Example A." (See '070 Pat., col. 9, ll. 14 – col. 10, ll. 13.) As noted, the method used is in accordance with the method described in Example A in International Patent Publication WO 96/01623. That method discusses increasing the optical purity of the magnesium salt via crystallization. (See '070 Pat., col. 9, ll. 31-47.)

As noted above, the parties each interpret the written description somewhat differently and argue that it supports their differing constructions. With respect to the claim term "the magnesium salt of S-omeprazole trihydrate," AstraZeneca argues that although the written description refers to crystalline and highly crystalline embodiments, it also describes "the magnesium salt of S-omeprazole trihydrate" generally, with no reference to crystallinity. (See dkt. 39 at 10-11.) AstraZeneca also points to the various testing methods for characterizing a trihydrate disclosed in the written description, arguing these methods do not require the trihydrate to be crystalline. (See id.) AstraZeneca further argues that the written description provides no lexicography or disavowal to alter the term's plain and ordinary meaning. (See dkt. 48 at 16-23.)

Andrx argues that the written description shows that the claimed trihydrate is crystalline and that the waters making it a trihydrate must be waters of crystallization. Specifically, Andrx points to the multiple statements regarding the "compound of the invention" found at column two of the '070 Patent. (See dkt. 38 at 13-14; dkt. 47 at 5-6.)[27]

Perrigo argues that statements found in column two of the written description also define the term "the magnesium salt of S-omeprazole trihydrate" as a "bulk product" and unequivocally disavow compositions containing substantial quantities of R-omeprazole

[27] On this point, Perrigo and Mylan are in agreement with Andrx. (See Perrigo action, dkt. 44 at 16-20; dkt. 50 at 19; Mylan action, dkt. 232 at 16-18; dkt. 244 at 8-12.)

magnesium and/or other physical forms of S-omeprazole magnesium, relative to any trihydrate that may be present.[28]

AstraZeneca characterizes these statements identified by the defendants as descriptions of claimed and unclaimed embodiments and examples. (See dkt. 48 at 17-22.)[29]

Andrx also argues that the only examples provided in the written description for making the claimed trihydrate (Examples 1 and 7) state that the product was obtained as crystals, not any amorphous form. (See dkt. 38 at 14.)[30] Thus, Andrx argues that forms other than crystalline forms were not contemplated by the inventors. AstraZeneca acknowledges the limited disclosure, but argues that defendants' positions call for the improper importation of limitations from the written description into the claims. (See dkt. 48 at 22-23.)

With respect to the term "characterized by the following major peaks in its X-ray diffractogram," AstraZeneca argues that the written description supports its construction because nothing in that written description requires the presence of every single peak

[28] (See Perrigo action, dkt. 44 at 16-20; dkt. 50 at 12-13, 15-16). Mylan argued that additional statements found in column two of the written description disavowed compounds that were not substantially pure. (See Mylan action, dkt. 232 at 16; dkt. 244 at 12-13.)

[29] Perrigo disagrees that the language AstraZeneca refers to as descriptions of claimed and unclaimed embodiments, and argues that it should be seen as unequivocally limiting the invention. (See Perrigo action, dkt. 50 at 17-18.)

[30] Mylan addresses the same examples, but their argument is slightly different, they consider the two crystalline examples to constitute a disclaimer of non-crystalline compounds. (See Mylan action, dkt. 232 at 18-19.)

identified in Figure 1 or Table 1. (See dkt. 39 at 14-17.) AstraZeneca also argues that the written description readily accounts for experimental error (an element of each of the defendants' proposed constructions) and inaccuracies in the claimed table of peaks. (See id. at 16.) Andrx and Perrigo both argue that the description of Example 1 explains that claim 1 of the '085 Patent is directed to a particular trihydrate form that exhibits exactly the 13 peaks recited in claim 1's table, and Andrx further argues that each peak must fall into the specified relative intensity range. (See dkt. 38 at 22-23.)[31]

With respect to the claim term "represented by Fig. 1," AstraZeneca argues that the written description does not require the stringent limitation "the same as" as proposed by each of the defendants – pointing to the "complies with" language in Example 7. (See dkt. 39 at 17-18.)[32] Perrigo and Andrx both argue that the written description fails to explain what is meant by "complies with" and that there is no XRPD data or a diffractogram for the product of Example 7, and that as a result, it should be interpreted as the "same as Figure 1." (See dkt. 38 at 28-29.)[33]

[31] (See Perrigo action, dkt. 44 at 29-30; dkt. 50 at 26-27.)

[32] Although AstraZeneca's argument relies on the "complies with" language found in the written description, Perrigo argues that AstraZeneca does not cite to any intrinsic evidence for its construction of this term. (See Perrigo action, dkt. 50 at 31.)

[33] (See Perrigo action, dkt. 44 at 32.)

c. Prosecution history of the '085 Patent

The relevant portions of the prosecution history of the '085 Patent have been supplied to the Court in the parties' Markman submissions. (Dkt. 38-1 at 30-88; dkt. 39-7; dkt. 48-11 to dkt. 48-13.)[34]

U.S. Patent Application No. 09/077719 (the "'719 Application"), which issued as the '085 Patent, was filed on June 8, 1998 by inventors Hanna Cotton, Anders Kronström, Anders Mattson, and Eva Möller (collectively "the Applicants"). ('085 Pat. at pg. 1.) The '719 Application is the National Stage Entry of International Application No. PCT/SE98/00974, filed May 25, 1998, which claims priority to Swedish Patent Application No. 9702065 filed May 30, 1997. (Id.) The '085 Patent was issued on April 9, 2002, so its prosecution process took approximately four years.

The docketed portions of the '085 Patent history begin in 1998 with the filing of the '719 Application. The '719 Application, as originally filed, included 16 claims. (Dkt. 38-1 at 53-57.) Claims 1-3 as originally filed are provided in the margin.[35] Claim 1

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[34] (See also Perrigo action, dkt. 44-6 to dkt. 44-12; id., dkt. 45-7; id., dkt. 50-5; id., dkt. 51-11 to dkt. 51-13; Mylan action, dkt. 230-7; id., dkt. 232-2 at 3-41; id., dkt. 245-11 to dkt. 245-13.) Some submissions in the Andrx, Perrigo, and Mylan actions were duplicative, whereas some of the submissions were not. The Court will discuss the prosecution history of the '085 Patent chronologically, utilizing many of the non-duplicative submissions of the parties, in an effort to paint a complete picture of the '085 Patent's prosecution history.

[35] **Claim 1**. The magnesium salt of S-omeprazole trihydrate.

Claim 2. The magnesium salt of S-omeprazole trihydrate according to claim 1, characterized by being highly crystalline.

Claim 3. The magnesium salt of S-omeprazole trihydrate according to claim 1 characterized by the following major peaks in its X-ray powder diffractogram:

of the '719 Application, as originally filed, is identical to issued claim 1 of the '070 Patent. This topic will be discussed in more detail in Section II.B.1.d, infra.

On November 27, 2000, in a first Office action, the examiner rejected claims 1-4, 14, 16 and 17[36] of the '719 Application under 35 U.S.C. § 103(a) (obviousness) as being unpatentable over:

1. U.S. Patent No. 4,738,974 (the "'974 Patent"), example 5 (dihydrate form of esomeprazole).
2. U.S. Patent No. 5,693,818 (the "'818 Patent"), examples 3-7.
3. International Patent Application Publication WO 95/01977 ("WO 95/01977"), page 3, lines 30-31 (for claim 4, see page 5, lines 7-8).
4. U.S. Patent No. 5,690,960 (the "'960 Patent"), examples 2, 4.

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d-value / Å	*Relative Intensity*
2.67	m
2.79	m
3.27	m
3.52	s
3.82	s
3.96	vs
4.14	m
5.2	m
5.6	m
6.7	vs
6.9	s
8.3	w
16.6	vs

(Dkt. 38-1 at 53).

[36] Claims 5-13 and 18 were withdrawn from further consideration, as Applicants elected to prosecute claims 1-4, 14, and 16-17 in response to a Restriction/Election Requirement. (See dkt. 38-1 at 70-72.)

5. U.S. Patent No. 5,900,424 (the "'424 Patent").

(Dkt. 38-1 at 68-73.) The examiner also rejected the claims "optionally" in view of Evans, An Introduction to Crystal Chemistry (1964) ("Evans") or Japanese Chemical Society, Experimental Chemical Seminar, Vol. 18 (1958) page 505 [sic] ("Japanese Chemical Society"). (Id. at 71.) The examiner asserted that "[a]ll references (except reference 1 [the '974 Patent – disclosing the dihydrate form]) disclose some form of magnesium salt of omeprazole without clearly specify[ing] water content." (Id.) The examiner asserted that "[t]he difference between the claims and the references' disclosure is that the claimed compound is S-form and trihydrate." (Id.) The examiner asserted that because the prior art references (except the '974 Patent) are "silent regarding the water content of the salt form, one having ordinary skilled [sic] in the art would have expected the [prior] art compound in the process of preparing inherently has water molecule attached." (Id. at 72.) The examiner went on to state:

> It is recognized in the art that organic solid material may include guest molecules to form crystals. However, the guest inclusion is mechanical in nature (see Evans p. 396), thus the instant claims are drawn to alternative form of a known compound. The alternative form is the innate nature for such a compound. Furhtermore [sic], the Japanese reference teaches that spontaneous resolution occurs in recrytlization [sic]. It is expected that if the crystalization [sic] solvent is water, then optical pure hydrate would result.

(Id.)

The examiner also rejected the pending claims for obvious-type double patenting in view of the '424 patent, the '974 Patent, and U.S. Patent No. 5,714,504 (the "'504 Patent"), and optionally in view of Evans or Japanese Chemical Society. (Id. at 72-73.)

The examiner took the position that the claims, although not identical, were not patentably distinct from each other because alternative forms of a known substance would be obvious. (See id. at 73.)

On April 26, 2001, the Applicants responded to the first Office action. (Dkt. 38-1 at 75-88; dkt. 39-7 at 2-5.) In their response, the Applicants provided the following recitation with respect to the claimed invention:

> The present invention is directed to a new and advantageous form of the magnesium salt of the (-)-enantiomer of omeprazole. As defined in the specification at page 3, line 3-9, the compound of the claimed invention is referred to as the magnesium salt of S-omeprazole trihydrate (**claim 1**). However, as used throughout this communication, the expressions "the (-)-enantiomer of omeprazole" and "S-omeprazole" will be used interchangeably. The claimed magnesium salt of S-omeprazole trihydrate is substantially free from magnesium salts of R-omeprazole and other prior art forms of magnesium salts of S-omeprazole, e.g., S-omeprazole magnesium dihydrate.
>
> At the time of the invention, it was not known that crystalline magnesium salt of the (-)-enantiomer of omeprazole occurred in structurally different forms. The claimed magnesium salt of S-omeprazole trihydrate is highly crystalline (**claim 2**) and is uniquely characterized by an X-ray powder diffractogram (**claim 3**) which distinguishes the claimed compound from any other form of the magnesium salt of S-omeprazole. As demonstrated by the comparative data set forth in the accompanying Declaration of Frans W. Langkilde (the "Declaration"), the claimed compound is more stable than the corresponding magnesium salt compounds of the prior art (**claim 17**).
>
> Applicants have surprisingly discovered that the claimed magnesium salt of S-omeprazole trihydrate is obtained by treating a magnesium salt of S-omeprazole of any other form, e.g., anhydrate, monohydrate, dihydrate, etc., with water (**claim 4**). Notwithstanding the different methods . . . by which

> the claimed compound is produced, Examples 1 and 7 of the specification show that the product of the different methods is characterized by the same X-ray powder diffractogram. In this regard, the Examiner's attention is directed to the following support: Example 1, Table 1 at page 9; Example 7 at page 17, lines 4-5; and Figure 1. In contrast and disadvantageously, the same degree of reproducibility is not obtained with the prior art dihydrate compound as shown in Examples 5 and 6 (See Figures 3 and 4).
>
> The demonstrated reproducibility and improved stability characterizing the claimed magnesium salt of S-omeprazole trihydrate renders the claimed compound particularly suitable as the active ingredient in full scale manufacturing processes of pharmaceutical formulations for treating gastric acid related conditions.

(Dkt. 38-1 at 79-80.) The Applicants also submitted a declaration of Dr. Frans W. Langkilde[37] (the "Langkilde Declaration"). (Dkt. 39-7 at 2-5.)

The Langkilde Declaration provided the following description of the claimed invention:

> Specifically, the invention is directed to a new and advantageous form of the magnesium salt of S-omeprazole. As stated in the specification at page 3, line 3-9, the compound of the claimed invention is referred to as the magnesium salt of S-omeprazole trihydrate. The claimed magnesium salt of S-omeprazole trihydrate is substantially free from magnesium salts of R-omeprazole and other prior art forms of magnesium salts of S-omeprazole.

(Dkt. 39-7 at 3.) The Langkilde Declaration also described a side-by-side comparison of certain physical chemical properties of "the claimed magnesium salt of S-omeprazole

[37] Dr. Frans W. Langkilde, Ph.D. is not an inventor of the '085 or '070 Patents. At the time of his declaration, Dr. Langkilde was employed by AstraZeneca as Group Leader, Analytical Development, Pharmaceutical and Analytical Research and Development. (Dkt. 39-7 at 3.)

trihydrate and S-omeprazole magnesium dihydrate of the prior art." The Langkilde Declaration concluded that the magnesium salt of S-omeprazole trihydrate was different than the prior art S-omeprazole magnesium salt dihydrate:

> The magnesium salt of S-omeprazole trihydrate is different when compared to the prior art S-omeprazole magnesium salt dihydrate. The solid state properties defining these forms are different. The claimed trihydrate is the more stable substance and, after storage of six (6) months or longer, is chemically more pure than the prior art dihydrate form. Furthermore, at the time the claimed invention was made, there was no suggestion that the magnesium salt of S-omeprazole existed in a trihydrate form. It was indeed surprising, therefore, to obtain the claimed compound and determine that the claimed magnesium salt of S-omeprazole trihydrate is more stable than the corresponding prior art compounds, thereby rendering the claimed trihydrate form more advantageous for use in pharmaceutical formulations.

(Id. at 4.)

The Applicants asserted that the Langkilde Declaration "demonstate[d] that the claimed compound is characterized by a superior and unexpected improvement in stability." (Dkt. 38-1 at 80.) Specifically, the Applicants stated that "[t]he comparative data [provided in the Langkilde Declaration] shows that the claimed magnesium salt of S-omeprazole trihydrate is more stable after 6 and 12 months than the prior art magnesium salt of S-omeprazole dihydrate. (Id.) The Applicants argued that the "improved physical and chemical properties that characterize the claimed compound" were not disclosed in the prior art and that the demonstrated improvement in stability represents a greater than expected result. (Id. at 80-81.) The Applicants also stated, with reference to the

Langkilde Declaration, that "the magnesium salt of S-omeprazole trihydrate is different when compared to the prior art magnesium salt of S-omeprazole dihydrate." (Id. at 81.)

With respect to the obviousness rejection under 35 U.S.C. § 103(a), the Applicants responded by arguing that none of the cited references (i.e., the '974 Patent, the '818 Patent, WO 95/01977, the '960 Patent, the '424 Patent, Evans, and Japanese Chemical Society) "suggest that there could be other crystalline forms of the magnesium salt of S-omeprazole" or "suggest that the claimed compound could be obtained by treating a magnesium salt of S-omeprazole of any other form with water." (Id.) The Applicants addressed and distinguished each of the cited references in turn. (See id. at 82-86.) The Applicants also argued that "it was unpredictable at the time the claimed invention was made whether the prior art compounds, when treated in an aqueous environment, would inherently have added water as a guest molecule in the crystals as a result of such a treatment." (Id. at 82.) The Applicants added that the "cited references fail to suggest the reproducibility and unexpected improvement in stability which characterize the claimed magnesium salt of S-omeprazole trihydrate as demonstrated by the Examples and [Langkilde] Declaration." (Id.)

With respect to the obvious-type double patenting rejection, the Applicants differentiated the '504 Patent and reiterated that the claimed compound was characterized by "superior and unexpected" improvements not suggested by the prior art:

> The '504 patent is a continuation-in-part of the cited '818 patent. The '504 patent claims the magnesium salt of the (-)-enantiomer of omeprazole. However, the '504 patent does not suggest that the magnesium salt of the (-)-enantiomer of omeprazole could exist in another more advantageous form,

> e.g., a trihydrate. Nor does the '504 patent suggest that the claimed magnesium salt of S-omeprazole trihydrate is more stable than the corresponding magnesium salt compounds of the prior art. Moreover, the Examples and [Langkilde] Declaration show that the claimed magnesium salt of S-omeprazole trihydrate is reproducible and more stable after 6 and 12 months than the prior art magnesium S-omeprazole compound.

(Id. at 86-87.)

On July 5, 2001, in a second Office action, the examiner again rejected claims 1, 2, 4, 14, 16 and 17. (See dkt. 48-11 at 2-6.) Specifically, the examiner rejected claims 1, 2, 4, 14, 16-17 under 35 U.S.C. § 103 as being "unpatentable over the art of record for the reasons of record." (Id. at 4.) With respect to the Langkilde Declaration, the examiner noted that it was carefully considered, but in the examiner's point of view it only applied to the "hydrate having the specific X-ray powder diffraction value as listed in claim 3." (Id.) The examiner suggested amending claim 1 to include the content of claim 3 to overcome the 35 U.S.C. § 103 rejection. (Id.) The examiner also noted that the obvious-type double patenting rejection would be overcome by such amendment. (Id.)

In that same second Office action, the examiner also provisionally rejected claims 1, 2, 4, 14, 16-17 as obvious under 35 U.S.C. § 103(a), based upon a presumption of future patenting of co-pending Application No. 09/690,044 (the "'044 Application"). (Id.)[38] A provisional obvious-type double patenting rejection over the '044 Application was also issued. (Id. at 5.)

[38] As discussed in more detail in Section II.B.1.e, infra, the '044 Application is a part of a related prior art patent family. The '044 Application issued as U.S. Patent No. 6,875,872.

On September 18, 2001, the Applicants responded to the second Office action. (See dkt. 48-12 at 2-9.) The Applicants amended claim 1 to incorporate the embodiment of claim 3, as suggested by the examiner.[39] (Id. at 2, 5.) The Applicants did not dispute the examiner's assertion that the Langkilde Declaration was "only relevant to the claimed compound having the X-ray powder diffractogram values as recited in claim 3." (See Id. at 6.) With respect to the rejections pertaining to the '044 Application, the Applicants argued that those rejections were mooted by the amendment of claim 1. (Id.)

On November 16, 2001, claims 1-2, 4-9, 14, 16-17 and 19 (renumbered as 1-12) were allowed. (See dkt. 48-13 at 2.) The examiner did not provide a statement of reasons for allowance in the Notice of Allowance, (see id. at 2); however, it is clear that the '719 Application was allowed based on the amendment of claim 1 to incorporate the embodiment of claim 3. On April 9, 2002, the '719 Application issued as the '085 Patent. ('085 Pat., pg. 1.)

As with the written description, the parties interpret the prosecution history of the '085 Patent differently, arguing that it supports each of their respective positions. AstraZeneca argues that the prosecution history makes clear that at the time of the invention, the trihydrate form of the magnesium salt of S-omeprazole was unknown – as evidenced by the absence of any prior art rejections over such a form. (See dkt. 39 at 11.) Perrigo disagrees, interpreting the November 27, 2000 Office action as including a prior

[39] The Applicants also amended claims 4, 5, 9, 14 and 16 to correct the recitation of claims from which they depended, canceled claims 3 and 18, and added new claim 19. (Id. at 3-5.)

art rejection and an acknowledgement by the examiner that the magnesium salt of S-omeprazole in the prior art contained at least some trihydrate.[40] Perrigo argues that the presence of some trihydrate in the prior art required the Applicants to respond to the first Office action and define "the magnesium salt of S-omeprazole trihydrate" as a bulk product, substantially free from R-omeprazole magnesium and other forms of S-omeprazole magnesium.[41] Perrigo also argues that the Applicants' remarks and arguments in response to the first Office action characterized the claimed trihydrate as crystalline.[42] Andrx likewise argues that the Applicants' remarks and arguments in response to the first Office action presume the crystallinity of the trihydrate. (See dkt. 38 at 14-15.)[43]

With respect to the claim term "characterized by the following major peaks in its X-ray diffractogram," Andrx argues that the prosecution history of the '085 Patent supports its proposed construction. Specifically, Andrx points to a statement by the Applicants in response to the first Office action, noting that Examples 1 and 7 show that the product is characterized by the same X-ray powder diffractogram. (See dkt. 38 at 23.)

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[40] (See Perrigo action, dkt. 44 at 22, 24-27; dkt. 50 at 14-15.)

[41] (See Perrigo action, dkt. 50 at 15.)

[42] (See Perrigo action, dkt. 50 at 19-20.)

[43] Mylan devotes substantial attention to this first Office action response as well. Mylan agrees with Andrx and Perrigo regarding the Applicants' emphasis of the crystallinity requirement. (See Mylan action, dkt. 232 at 19-20; dkt. 244 at 13-14.) Mylan also argues that the Applicants' remarks and arguments in that Office action response support its construction that the claimed compound be "substantially pure." (See Mylan action, dkt. 232 at 19-20; dkt. 244 at 13-14.)

Andrx argues that this statement amounts to an understanding by the Applicants that the term "complies with" and "characterized by" are interchangeable. (Id.) Perrigo argues that the Applicants' response to the first Office action relied on the XRPD to distinguish the claimed invention from the prior art, and as a result, the term at issue should be required to include each of the major peaks.[44, 45]

d. Prosecution history of the '070 Patent

The relevant portions of the prosecution history of the '070 Patent have been supplied to the Court in the parties' Markman submissions. (Dkt. 38-1 at 90-168; dkt. 39-8 to dkt. 39-10; dkt. 48-14 to dkt. 48-16.)[46]

U.S. Patent Application No. 10/672,936 (the "'936 Application") was filed on September 25, 2003 and issued as the '070 Patent on August 12, 2008. ('070 Pat. at pg. 1.) The '936 Application is a continuation application of U.S. Patent Application No. 10/076,711, filed February 14, 2002, which is a divisional application of the '719 Application.

The docketed portions of the '070 Patent history begin in 2003 with the filing of the '936 Application. A Preliminary Amendment was filed concurrently with

[44] (See Perrigo action, dkt. 44 at 30; dkt. 50 at 27-28.) Perrigo also puts forth essentially the same argument and relies on the prosecution history of the '085 Patent for its construction of the claim term "Represented by FIG. 1" in the '070 Patent. (See Perrigo action, dkt. 44 at 32-33.)

[45] Mylan's argument was consistent with Perrigo's on this point. (See also Mylan action, dkt. 244 at 30-32.)

[46] (See also Perrigo action, dkt. 44-13 to dkt. 44-22; id., dkt. 45-8 to dkt. 45-10; id., dkt. 51-14 to dkt. 51-16; Mylan action, dkt. 230-8 to 230-10; id., dkt. 232-2 at 43-96; id., dkt. 245-14 to dkt. 245-16; id., dkt. 247-5.)

the '936 Application, leaving five claims for prosecution.[47] Those five claims are provided in the margin.[48] The Applicants[49] included the following remarks regarding the preliminary amendment to the claims and their relationship to the '719 Application:

> The claimed matter of the subject application is directed to those embodiments which were cancelled in the grandparent application '719 application [sic] for the sake of advancing the '719 application to allowance. Specifically, during the examination of the '719 application, the claims were limited to the embodiment or [sic: of] original claim 3. The '719 application thereafter matured into the '085 patent.
>
> Applicants submit that the limitation of the claimed subject matter of the '719 application to the embodiment of original claim 3 was not done in acquiescence of any objection or rejection relating to patentability of the canceled claims or deleted embodiments. Rather, the claims of the '719 application were so amended to advance the '719 application to allowance so that Applicants could enjoy the benefits,

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[47] (Perrigo action, dkt. 44-13 at 2-6.)

[48] **Claim 1.** The magnesium salt of S-omeprazole trihydrate.

Claim 2. The magnesium salt of S-omeprazole trihydrate according to claim 1, wherein the compound is in a highly crystalline form.

Claim 14. A pharmaceutical composition comprising the magnesium salt of S-omeprazole trihydrate according to claim 1 or 2 as active ingredient in association with a pharmaceutically acceptable carrier.

Claim 17. The pharmaceutical composition according to claim 14 further comprising one or more therapeutically active ingredients.

Claim 18. A method of treating a gastric acid related condition which method comprises administering to a subject suffering from said condition a therapeutically effective amount of the magnesium salt of S-omeprazole trihydrate according to claim 1 or 2.

(Perrigo action, id.)

[49] The "Applicants" of the '936 Application were identical to the '719 Application, and were inventors Hanna Cotton, Anders Kronström, Anders Mattson, and Eva Möller.

> without delay, conferred by a U.S. patent for allowable subject matter.
>
> Therefore, by this continuation application, Applicants wish to resume examination of the claimed subject matter of the '719 application that was previously canceled or deleted. Applicants submit that they are entitled to patent protection as broadly supported by the application as originally filed. As such, the pending claims of this continuation application are directed to the magnesium salt of S-omeprazole trihydrate, pharmaceutical compositions comprising the magnesium salt of S-omeprazole trihydrate, a pharmaceutically acceptable carrier and optionally one or more additional active ingredients and methods of treating gastric related condition [sic] by administering the claimed compounds.[50]

On July 16, 2004, in a first Office action, the examiner rejected claims 1, 2, 14, 17 and 18 under 35 U.S.C. § 103 (obviousness) as being unpatentable over International Patent Application Publication WO 94/27988 to Lindberg ("Lindberg").[51] Specifically, the examiner asserted that Lindberg disclosed the magnesium salt of S-omeprazole and "improved pharmacokinetic and metabolic properties of pure enantiomers of omeprazole," but did not disclose a trihydrate form.[52,53] The examiner concluded that "in absence of some unexpected superior efficacy of instant trihydrate over the prior art known magnesium salt of S-omeprazole, it would have been obvious to one skilled in the

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[50] (Perrigo action, dkt. 44-13 at 5-6.)

[51] (Perrigo action, dkt. 44-14 at 3-6.)

[52] (Id. at 5.)

[53] As discussed in Section II.B.1.b, supra, the inventors acknowledged that the magnesium salt of S-omeprazole was known in the prior art, as evidenced by the identification and discussion of the Lindberg reference in the Background section of the written description. See '070 Pat., col. 1, ll. 35-55.

art to prepare hydrates of magnesium salt of S-omeprazole without affecting its utility for treating ulcer."[54] The examiner also rejected claims 1, 2, 14, 17 and 18 under 35 U.S.C. § 103 as being unpatentable over International Patent Application Publication WO 96/01623 to Bergstrand ("Bergstrand") for reasons similar to that of Lindberg.[55] The examiner also rejected claims 1, 2, 14, 17 and 18 under 35 U.S.C. § 101 (statutory double patenting) as claiming the same invention as that of claims 1, 2, 11 and 12 of the '085 Patent.[56]

On December 15, 2004, the Applicants responded to the first Office action.[57] In their response, the Applicants explained that: "The present invention is directed to the magnesium salt of the (-)-enantiomer of omeprazole. As defined in the written description at page 3, line 3-9, the compound of the clamed invention is referred to as the magnesium salt of S-omeprazole trihydrate."[58] With respect to the obviousness rejections, the Applicants responded by arguing that the claimed invention was non-obvious in view of Lindberg and Bergstrand because neither Lindberg or Bergstrand suggested that another form of magnesium salt of S-omeprazole was possible.[59] With

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[54] (Perrigo action, dkt. 44-14 at 5-6.)

[55] (Id.) The Bergstrand reference was also identified and discussed by the inventors in the Background section of the written description. (See '070 Pat., col. 1, ll. 55-58.)

[56] (Id. at 6-7.)

[57] (See Mylan action, dkt. 232-2 at 51-55.)

[58] (Id. at 52.)

[59] (Id. at 54.)

respect to the double patenting rejection under 35 U.S.C. § 101, the Applicants responded that the scope of the claims of the '085 patent was different from the scope of the claims of the '936 Application, as evidenced by the express language of the claims.[60]

On April 29, 2005, in a second Office action, the examiner maintained the rejections of claims 1, 2, 14, 17 and 18 under 35 U.S.C. §§ 101 and 103.[61] With respect to those rejections, the examiner provided the following comments:

> In regard to obviousness rejections, the examiner does not agree with the applicants arguments also since the utility is identical. The applicants did not provide any unexpected data or superior activity of the instant trihydrate or crystalline form as compared to known magnesium salt of S-omeprazole of the two cited references. What is the evidence that the trihydrate or crystalline form is maintained in the pharmaceutical composition or following in vivo administration of magnesium salt of S-omeprazole? In regard to double patenting rejection, the examiner does not agree with the applicants arguments that the scope is different. The applicants did not provide any reasons or provided any evidence to show how the scope is different? Are the major peaks in X-ray diffractogram different in the instant magnesium salt of S-omeprazole as compared to the cited patent?[62]

On October 28, 2005, the Applicants responded to the second Office action.[63] With respect to the statutory double patenting rejection under 35 U.S.C. § 101, the Applicants argued that "[c]laims 1, 2, 14 and 18 of the ['719 Application] and claims 1,

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[60] (Id.)

[61] (See Perrigo action, dkt. 44-15 at 2-6.)

[62] (Id. at 4.)

[63] (See Perrigo action, dkt. 44-16 at 2-9.)

2, 11 and 12 of the '085 patent are related as genus and species, respectively" and that as a result there is no identity of invention between them.[64] With respect to the obviousness rejection, the Applicants argued that although the dihydrate of S-omeprazole magnesium salt was known at the time of the claimed invention, the prior art did not suggest the claimed trihydrate form of the magnesium salt of S-omeprazole.[65] The Applicants also argued that neither Lindberg nor Bergstrand suggested "the claimed magnesium salt of S-omeprazole trihydrate is more stable than the corresponding magnesium salt compounds of the prior art" and that the "demonstrated improvement in stability represents a greater than expected result."[66]

On November 21, 2005, in a third Office action, the examiner again rejected claims 1, 2, 14, 17, and 18, maintaining the obviousness and double patenting rejections.[67] With regard to the obviousness rejection, the examiner argued that the utility was identical and the Applicants had failed to provide any data of superior activity or physical properties that would distinguish the trihydrate from the dihydrate form.[68] With regard to the double patenting rejection, the examiner maintained that the pending

[64] (Id. at 5-6.)

[65] (Id. at 6-8.)

[66] (Id. at 8-9.)

[67] (See Perrigo action, dkt. 44-17 at 2-4.)

[68] (Id.)

claims and cited '085 Patent were the same, and asserted that the Applicants did not provide any differentiation.[69]

On May 19, 2006, the Applicants responded to the third Office action, canceling claims 14, 17 and 18 so that the only claims remaining were claims 1 and 2.[70] The Applicant summarized the content of an examiner interview, indicating that the examiner clarified that the 35 U.S.C. § 103 (obviousness) rejection applied only to claims 14 and 17 (now moot, due to the cancelation of those claims).[71] With respect to the statutory double patenting rejection under 35 U.S.C. § 101, the Applicants argued that the act of rewriting original claim 3 of the '085 patent in independent form during the prosecution of the '085 Patent is an acknowledgement that the claim scope of pending claim 1 and claim 1 of the '085 patent must be different and have a species and genus relationship.[72]

On August 10, 2006, in a fourth Office action, the Examiner maintained the statutory double patenting rejection of claims 1 and 2, again asserting that claims 1 and 2 were identical to claim 1 of the '085 Patent. (Dkt. 39-8 at 2-5.) The Applicants appealed the examiner's decision. (See dkt. 39-9 at 2-11.) Applicants' Appeal Brief provided the following summary of the claimed subject matter:

> Esomeprazole (S-omeprazole) is the (-)-enantiomer of 5-methyoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-

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[69] (Id.)

[70] (See Mylan action, dkt. 232-2 at 69-73.)

[71] (Id. at 71.)

[72] (Id. at 71-72.)

> methyl]sulfinyl]-1H-benzimidazole (specification at p. 1, lines 4-5).
>
> Claim 1 is the only independent claim. As defined by claim 1, the claimed invention is directed to the magnesium salt of S-omeprazole trihydrate (specification at p. 1, lines 6-7). At the time the claimed invention was made, it was not known that the magnesium salt of S-omeprazole occurs in a number of structurally different forms (specification at p. 3, lines 3-4). The compound of the invention is advantageous because it is more stable than the corresponding magnesium salt compounds of S-omeprazole in the prior art and, therefore, it is easier to handle and store (specification at p. 3, lines 11-13).

(Id. at 4.) With respect to the statutory double patenting rejection under 35 U.S.C. § 101, the Applicants again argued that a comparison of the prosecution history of the '085 Patent confirmed that pending claims 1 and 2 were different in scope than claims 1 and 2 of the '085 Patent. (Id. at 4-10.) The Applicants concluded that argument as follows:

> The quoted statements from the prosecution history of the '085 patent evidence the PTO's position and how the Examiner understood the claimed invention. Specifically, the Examiner understood there to be a difference in scope between original claim 1 directed to the magnesium salt of S-omeprazole trihydrate and original claim 3 referring back to and further limiting claim 1. To advance the '719 application to allowance and to enjoy the benefits conferred by a U.S. patent for allowable subject matter, claim 1 of the '719 application was amended to recite the X-ray powder diffraction values of claim 3 which was then canceled. The § 103 and obviousness-type double patenting rejections were withdrawn and the '085 patent was granted.
>
> Since it was the PTO's position that original claim 3 of the '719 application referred back to and further limited the subject matter of claim 1 of the '719 application in satisfaction of 35 U.S.C. § 112, ¶4, and the related regulation 37 C.F.R. § 1.75(c), then for the same reason claim 1 of the '085 patent must be limited or narrower in scope than claim 1 of the subject application. The PTO cannot now change its position since

> Applicants previously relied on the PTO and amended the claims accordingly.

(Id. at 9.)

The appeal portion of the prosecution history abruptly ceased following the filing of the appeal. The next event that appears in the docketed submissions is an August 14, 2007 Office action, the fifth Office action issued by the examiner. In that fifth Office action, the examiner withdrew the statutory double patenting rejection under 35 U.S.C. § 101,[73] but the examiner issued an obvious-type double patenting rejection of claims 1 and 2. (See dkt. 39-10 at 2-6.) The examiner also rejected claim 2 under 35 U.S.C. § 112 as being indefinite because the meaning of the term "highly crystalline form" was allegedly unclear. (Id. at 4.)[74]

[73] The examiner noted that the Final Rejection was withdrawn in view of an appeals conference in response to Applicants' appeal brief, but the examiner did not provide details or a summary of the appeals conference. (See dkt. 39-10 at 4.)

[74] Specifically, the examiner stated:

> In claim 2, the term --- highly crystalline form --- is indefinite since its meaning is not clear. According to the specification on page 4, first paragraph, this term is defined as --- having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art ----. This does not tell anything about the crystallinity of instant trihydrate form since there is no comparative data present as compared to prior art known forms including trihydrate form (see line 5 page 4). Does the instant trihydrate form has [sic] higher crystallinity as compared to the trihydrate form of Pat 6,669,085?

(Dkt. 39-10 at 2-6.)

On September 21, 2007, the Applicants responded to the fifth Office action.[75] The Applicants added claims 20 and 21, which are provided in the margin.[76] The Applicants canceled claim 2, mooting the rejection under 35 U.S.C. § 112.[77] To overcome the obvious-type double patenting rejection, the Applicants filed a terminal disclaimer over the '085 Patent.[78]

On December 6, 2007, the Applicants filed a supplemental amendment, amending claim 20 to correct antecedent basis, canceling claim 21, and adding new claims 22 and 23, which are provided in the margin.[79]

On December 7, 2007, the examiner issued a notice of allowance, allowing claims 1, 20, and 21. (See dkt. 48-16 at 2-3.) It appears that the examiner issued this notice of allowance prior to reviewing the contents of the supplemental amendment. On March 4,

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[75] (See Perrigo action, dkt. 44-19 at 2-6.)

[76] **Claim 20**. The magnesium salt of S-omeprazole trihydrate according to claim 1 represented by the Figure 1.

Claim 21. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim 1 or 20 which comprises treating a magnesium salt of S-omeprazole of any other form with water. (Perrigo action, dkt. 44-19 at 3.)

[77] (Perrigo action, dkt. 44-19 at 3-4.)

[78] (Id. at 4, 6.)

[79] **Claim 22**. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim 1 which comprises treating a magnesium salt of S-omeprazole of any other form with water.

Claim 23. A process for the preparation of the magnesium salt of S-omeprazole trihydrate according to claim 20 which comprises treating a magnesium salt of S-omeprazole of any other form with water. (Perrigo action, dkt. 44-20 at 2-4.)

2008, the examiner issued a supplemental notice of allowability allowing claims 1, 20, 22 and 23 in response to the December 6, 2007 supplemental amendment.[80] On August 12, 2008, the '936 Application issued as the '070 Patent. ('070 Pat., pg. 1.)

Again, the parties each argue that the prosecution history of the '070 Patent supports their respective positions. AstraZeneca argues that claim 1 of the '085 Patent and claim 1 of the '070 Patent must have a different scope because AstraZeneca was able to overcome the statutory double patenting rejection, arguing that claim 1 of the '070 Patent was different and broader than claim 1 of the '085 Patent. (See dkt. 39 at 11-12.) Perrigo acknowledges this, but argues that the withdrawal of this rejection does not warrant interpreting claim 1 of the '070 Patent beyond that allowed by the written description or its prosecution history.[81] AstraZeneca also argues that nothing in the prosecution history of the '070 Patent constitutes a disavowal or disclaimer of the scope of the term "the magnesium salt of S-omeprazole trihydrate" in claim 1 of the '070 Patent, and therefore AstraZeneca argues that any statements made in the prosecution history of the '085 Patent should not limit the '070 Patent claims. (See dkt. 48 at 23-25.)

Andrx argues that the Applicants' remarks and arguments in response to the October 28, 2005 Office action were premised on the notion that the waters defining the trihydrate were indeed waters of crystallization that conferred a unique structure to the claimed trihydrate. (See dkt. 38 at 15.)

[80] (See Perrigo action, dkt. 44-22 at 2-5.)

[81] (See Perrigo action, dkt. 50 at 22-23.)

e. Related prior art patent family

As discussed in Section II.B.1.c, supra, the '719 Application (which became the '085 Patent) was subject to an obvious-type double patenting rejection in view of multiple patents, including the '504 Patent.[82] The '504 Patent is assigned to Astrazeneca AB, the same assignee as the '085 and '070 Patents. The '504 Patent is an expired patent also covering the Nexium® product. The '504 Patent is a continuation-in-part of U.S. Patent Application No. 08/256,174 filed June 28, 1994, which issued as U.S. Patent No. 5,693,818, which was the national stage entry of International Patent Application No. PCT/SE94/00509, filed May 27, 1994, which claimed priority to Swedish Patent Application No. 9301830-7. This family of patents[83] also includes the following issued, but expired patents: U.S. Patent Nos. 5,877,192 (the "'192 Patent"), 6,875,872 (the "'872 Patent")[84], and 6,143,771 (the "'771 Patent"). (See dkt. 105.)

The '504 Patent claimed pharmaceutical formulations (and treatment methods) comprising solid, chemically pure alkaline salts of the S-enantiomer of omeprazole and a pharmaceutically acceptable carrier. This patent is further limited to "optically pure" alkaline salts of the S-enantiomer of omeprazole (claim 2); specific alkaline salts, such as

[82] A copy of the '504 patent was submitted by Mylan and can be found at Mylan action, dkt. 232-10.

[83] A diagram of this patent family tree illustrating the relationships among these patents was prepared by the Court for convenience and may be found at dkt. 105.

[84] A copy of the '872 patent was submitted by Mylan and can be found at Mylan action, dkt. 232-11.

magnesium or sodium (claims 3 and 5); and salts in a "substantially crystalline form" (claim 4). Claims 6 through 10 are directed to methods of using the claimed formulation.

The '192 Patent claimed methods for treating gastric acid related diseases with the S-enantiomer of omeprazole to achieve certain biological benefits (claims 1 and 2), and a method for the production of an S-enantiomer of omeprazole-containing medicament for treating gastric diseases (claim 12). Other claims of the '192 Patent recite additional improved properties of the S-enantiomer of omeprazole (claims 3-6 and 13-18), specific administration methods and dosage amounts (claims 7-11 and 13-22), and an enantiomeric purity limitation (claim 23).

The '872 Patent claimed the magnesium salts of the S-enantiomer of omeprazole exhibiting high or very high optical purities of "at least about": 94% (claim 1), 98.4% (claim 4), 99.8% (claim 7), and 99.9% (claim 10), measured by enantiomeric excess (commonly abbreviated as "ee"). Claims 2, 5, 8, and 11 are parallel to claims 1, 4, 7, and 10, only the "about" language is removed. Claims 3, 6, and 9 limit the independent claims to those containing the magnesium salt of the S-enantiomer of omeprazole "in crystalline form."

The '771 Patent claimed pharmaceutical formulations comprising an optically pure solid state sodium salt of the S-enantiomer of omeprazole as the active ingredient (claims 1, 2) and methods of treating gastrointestinal inflammatory diseases and conditions with the same (claims 6, 7, 11, 12). Claim 3 limits the sodium salt of the S-enantiomer of omeprazole to a substantially crystalline form. Claims 4, 5, and 8-10 further limit the pharmaceutical formulation.

The Court notes that the '504, '192 and '872 Patents have been the subject of extensive prior litigation in this Court and have been the subject of multiple claim construction opinions. See, e.g., AstraZeneca AB v. Dr. Reddy's Laboratories, Ltd., No. 05-5553, 2010 WL 1981790 (D.N.J. May 18, 2010) (construing terms of the '504, '192, and '872 Patents); AstraZeneca AB v. Dr. Reddy's Laboratories, Inc., Nos. 11-2317, 11-4275, 11-6348, 2013 WL 1847639 (D.N.J. May 1, 2013) (construing terms of the '504 and '872 Patents, among others); Astrazeneca AB v. Hanmi USA, Inc., No. 11-760, 2012 WL 6203602 (D.N.J. Dec. 12, 2012) (construing terms of the '504 and '192 Patents), aff'd 554 Fed. Appx. 912 (Fed. Cir. 2013).

3. Summary of extrinsic evidence

This subsection summarizes the expert positions and exhibits on claim construction issues.[85] Our analysis will follow in Section II.B.4. The organization of this subsection is explained in the margin.[86]

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[85] To the degree expert witnesses addressed intrinsic evidence and stated their view as to how a POSA would interpret the intrinsic evidence, it appears that the Court's analysis of those portions could be subject to clear error review, rather than *de novo* review. See Teva Pharm. USA, Inc. v. Sandoz, Inc., 135 S. Ct. 831, 837-38 (2015). We express no view on that issue.

[86] This subsection, Section II.B.3, summarizes the extrinsic claim construction evidence. That evidence consists of filed submissions, including declarations and deposition testimony of expert witnesses. Some portions of the docketed deposition testimony were filed by the opposing party. (See, e.g., dkt. 47-1 at 4-25 (excerpts of deposition of plaintiff's expert, filed by defendant Andrx); dkt. 48-3 at 2-34 (excerpts of deposition of defendant Perrigo's expert, filed by plaintiff); dkt. 48-6 at 2-23 (excerpts of deposition of defendant Andrx's expert, filed by plaintiff).)

Plaintiff identifies one expert witness, Dr. Stephen Byrn. In each action, plaintiff filed two declarations of Dr. Byrn. (Dkt. 40; dkt. 49; Perrigo action, dkt. 46; dkt. 52; Mylan action, dkt. 231; dkt. 246.) Dr. Byrn's first declaration in each case was nearly identical. (See dkt. 40;

a. Plaintiff's expert testimony and exhibits

Dr. Byrn was presented by plaintiff as an expert in the field of solid state chemistry, including the analysis of the form, stability, solvates, and polymorphs of drugs. His qualifications are summarized in the margin.[87] Dr. Byrn provided testimony on the claim terms "the magnesium salt of S-omeprazole trihydrate," "characterized by the following major peaks in its X-ray diffractogram," and "represented by FIG. 1."

i. "The magnesium salt of S-omeprazole trihydrate"

To review, AstraZeneca proposes that the claim term "the magnesium salt of S-omeprazole trihydrate" be construed as follows: "a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-

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Perrigo action, dkt. 46; Mylan action, dkt. 231). Dr. Byrn's second declaration in each case was also nearly identical. (See dkt. 49; Perrigo action, dkt. 52; Mylan, action, dkt. 246)

Andrx identifies one expert witness, Dr. Michael Zaworotko. In the Andrx action, Andrx filed three declarations of Dr. Zaworotko. (Dkt. 38-3 at 1-29; dkt. 47-2; dkt. 54-1 at 1-6.)

Perrigo identifies one expert witness, Dr. Graham Buckton. In the Perrigo action, Perrigo filed two declarations of Dr. Buckton. (Perrigo action, dkt. 44-1; dkt. 50-1.)

Mylan identified two expert witnesses, Dr. Jerry Atwood and Dr. Robert R. Ruffolo. In the Mylan action, Mylan filed three declarations of Dr. Atwood (Mylan action, dkt. 232-16; dkt. 247-6; dkt. 269-1), and two declarations of Dr. Ruffolo. (Id., dkt. 232-18; id., dkt. 247-7.)

The organization of this subsection is as follows: Section II.B.3.a summarizes the evidence from plaintiff's expert, Dr. Byrn. Section II.B.3.b summarizes the evidence from Andrx's expert, Dr. Zaworotko. Section II.B.3.c summarizes the evidence from Perrigo's expert, Dr. Buckton. A summary of the evidence from Mylan's experts is not provided, but when appropriate, reference is made to such evidence in the margin.

[87] Dr. Byrn has qualifications as a university professor in various positions in the areas of pharmaceutical and solid state chemistry since 1972. (Dkt. 40 at 2.) He has published two books and over 170 articles on the subject of solid state chemistry. (Id.) He has also served as a consultant to various entities within the pharmaceutical community. (Id. at 2-3.)

omeprazole." (Dkt. 36 at 3.) Dr. Byrn declared that the POSA would understand the phrase "the magnesium salt of S-omeprazole trihydrate," as used in the claims of the '085 and '070 Patents, to have three characteristics: "a magnesium salt; of the S-omeprazole enantiomer; and a trihydrate." (Dkt. 40 at 6.) There appears to be no disagreement among the experts regarding the term "a magnesium salt," or the term "S-omeprazole," which Dr. Byrn explained means the S- or (-)-enantiomer of omeprazole. The disagreement in this matter concerns the term "trihydrate" and its meaning to the POSA at the time of the invention.

In Dr. Byrn's opinion, the POSA would understand the term "trihydrate," as describing a compound having three molecules of bound water per every molecule of the magnesium salt of S-omeprazole. (Id.) His definitions and understandings differ from that of the other experts in that Dr. Byrn does not limit the trihydrate to a crystalline form. Specifically, Dr. Byrn opined that a POSA would not understand the term "the magnesium salt of S-omeprazole trihydrate" to be limited to a crystalline form. In the context of claim 1 of the '070 Patent, he opined that the POSA would understand that term to "cover esomeprazole magnesium trihydrate of any degree of crystallinity, and to cover esomeprazole magnesium trihydrate in any amount, even if it is mixed with a different form of esomeprazole magnesium." (Id. at 7-8.)

It is Dr. Byrn's opinion that a hydrate need not be crystalline, it must merely have some structure that "can bind water in a regular way." (Id.)[88] He explained that the term hydrate "differentiates a compound from other substances in which the water present is loosely associated or only present on the surface." (Id.) To support his opinion that the term "hydrate" is not limited to a crystalline form, Dr. Byrn declared that the existence of amorphous hydrates, in general, were well known at the time of the invention. (Id.)[89] As pointed out by Dr. Zaworotko, and discussed in more detail in Section II.B.3.b, infra, the references cited by Dr. Byrn for this proposition are after the May 30, 1997 priority date

[88] Dr. Byrn does acknowledge that hydrates may be crystalline, i.e., water may be "bound" or incorporated into the crystal lattice of a drug substance's unit cell. This example originates from a paper he co-authored, Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations, 12 Pharmaceutical Research 945, 946 (1995) (dkt. 40-8). That paper provides a description of polymorphs, hydrates (solvates), desolvated solvates, and amorphous forms:

> "Polymorphs exist when the drug substance crystallizes in different crystal packing arrangements all of which have the same elemental composition (Note that hydrates can exist in polymorphs). Hydrates exist when the drug substance incorporates water in the crystal lattice in either stoichiometric or non-stoichiometric amounts. Desolvated solvates are produced when a solvate is desolvated (either knowingly or unknowingly) and the crystal retains the structure of the solvate. Amorphous forms exist when a solid with no long range order and thus no crystallinity is produced."

(Dkt. 40-8 at 3.)

[89] The references cited by Dr. Byrn to support his opinion on this point were: Megarry, et al., Amorphous trehalose dihydrate by cryogenic milling, 346 Carbohydrate Research 1061-64 (2011) ("Megarry") (dkt. 40-9); U.S. Patent No. 7,638,634, titled "Amorphous Esomeprazole Hydrate" ("the '634 Patent") (dkt. 40-10); U.S. Patent No. 7,244,842, titled "Amorphous Hydrate of a Cephalosporin Antibiotic" ("the '842 Patent") (dkt. 40-11); and International Patent Publication No. WO 04/020436, titled "Amorphous Hydrates of Esomeprazole Magnesium and Process for the Preparation Thereof ("WO 04/02036") (dkt. 40-12).

of the '085 and '070 Patents, and thus are not evidence of what was known at the time of the invention. (See dkt. 47-2 at 4-6.) Dr. Byrn acknowledged this in his second declaration, and cited six additional references which he asserted provide examples of amorphous hydrates at the time of the invention. (See dkt. 49 at 6-7.)[90] Dr. Zaworotko again took issue with these additional references and opined that they are irrelevant to the scientific field to which the '085 and '070 Patents pertain. See Section II.B.3.b, infra. Dr. Byrn also cited two dictionary definitions for the term "trihydrate" to support his opinion that the compound need not be limited to a crystalline form. (Id. at 8.)[91] Neither of those definitions include a definitional crystallinity requirement.

Beyond amorphous hydrates in general, Dr. Byrn also stated that amorphous forms of the magnesium salt of S-omeprazole were known, citing International Patent

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[90] The additional references cited by Dr. Byrn were: Peter S. Belton, An ^{1}H Pulsed N.m.r. Study of Some Amorphous Silicate Hydrates, 29 J. Chem. Tech. Biotechnol. 19-25 (1979) ("Belton") (dkt. 49-2); Delzeit, et al., Infrared Spectra of HCl Complexed/Ionized in Amorphous Hydrates and at Ice Surfaces in the 15-90 K Range, 97 J. Phys. Chem. 10312-10318 (1993) ("Delzeit") (dkt. 49-3); H. Neil McMurray, Hydrothermal Modification of Electrocatalytic and Corrosion Properties in Nanosize Particles of Ruthenium Dioxide Hydrate, 4(8) J. Mater. Chem., 1283-1287 (1994) ("McMurray") (dkt. 49-4); Koch, et al., Low-Temperature Photochemistry of Submicrometer Nitric Acid and Ammonium Nitrate Layers, 100 J. Phys. Chem. 11402-11407 (1996) ("Koch") (dkt. 49-5); Kalceff, et al., Cathodoluminescence Microanalysis of Natural Hydrated Amorphous SiO_2; Opal, 24 Phys. Chem. Minerals 131-138 (1997) ("Kalceff") (dkt. 49-6); U.S. Patent No. 5,395,602, titled "Method for the Production of Sodium Perborate Hydrate Granulates ("the '602 Patent") (dkt. 49-7).

[91] The 2002 Merriam-Webster's Medical Desk Dictionary defines "trihydrate" as "a chemical compound with three molecules of water." (Dkt. 40-14 at 5.)

The 1989 Oxford English Dictionary defines "trihydrate" as "[a] compound containing three molecules of water combined with an element or radical or with another compound." (Dkt. 40-15 at 4.)

Publication No. WO2004/020436. (See dkt. 40 at 7.) Andrx took issue with this assertion, noting that the language "amorphous hydrates of S-omeprazole magnesium," appearing in this publication was error, acknowledged by both the USPTO and applicants by way of certificate of correction filed in U.S. Patent No. 7,612,098. (See dkt. 86-1 at 4-5,10-22.) Specifically, the term "hydrate of" was replaced with "hydrous" throughout the '098 Patent. (See id. at 21-22.)

Dr. Byrn also opined that a POSA would understand that water can be present in a regular arrangement (i.e., short range order) in solid magnesium compounds, without the formation of a crystalline structure, by forming a hydrophilic layer that incorporates water molecules. (Dkt. 40 at 7.)[92] He also stated that processes for making a crystalline material amorphous, such as milling, grinding, or granulating, were within the knowledge of a POSA. (Id.) He explained that the POSA would understand these techniques could be applied to the magnesium salt of S-omeprazole trihydrate to make it amorphous. (Id.)

Dr. Byrn cited intrinsic evidence of record (i.e., the written description, the prosecution histories of the '085 and '070 Patents, and the Langkilde Declaration) supporting his position. He explained that, based on his review of the prosecution histories, the novelty of the inventions of both the '085 and '070 Patents was in the discovery of the trihydrate form of the magnesium salt of S-omeprazole, which was not

[92] As evidence, he cited T. Egami & S.J.L. Billinge, Underneath the Bragg Peaks: Structural Analysis of Complex Materials, 12 (R.W. Cahn ed., 2003.)

limited to a specific state (i.e., crystalline or amorphous). (Id. at 8.)[93] He acknowledged a POSA would understand claim 1 of the '085 Patent, which is defined by a particular list of X-ray powder diffraction peaks, to be narrower than claim 1 of the '070 Patent, but he asserted that claim 1 of the '085 Patent is still not limited to form or amount. (Id. at 8-9.)[94] He interpreted the written description's statements regarding the "invention" and the "compound of the invention" found at column 2 of the '070 Patent, discussed in Section II.B.1.b, supra, as non-limiting. It was Dr. Byrn's position that any language in the patent referring to the invention being crystalline or highly crystalline would not be understood by a POSA as inherent limitations in the claims because the POSA would understand these statements as describing different example compounds and preferred embodiments made pursuant to the specific examples set forth in the written description. (See id. at 9-10.)

When discussing the opposing construction positions of the parties, Dr. Byrn again emphasized that, in his opinion, a POSA would not understand non-crystalline forms of the magnesium salt of S-omeprazole trihydrate to be excluded from claim 1 of the '070

[93] For example, he pointed to the following statement in the Langkilde Declaration: "at the time the claimed invention was made, there was no suggestion that the magnesium salt of S-omeprazole existed in a trihydrate form." (Dkt. 40 at 8, citing dkt. 40-4 at 4.)

[94] It is not clear to the Court what Dr. Byrn means by the term "form" in this context. The Court notes that AstraZeneca admitted, in its written submissions, that claim 1 of the '085 patent is limited to a crystalline form. (See dkt. 39 at 8 ("The tabulated peaks of claim 1 are indicative of crystalline material. So, Defendants' attempt to read a separate crystallinity limitation into 'trihydrate' would be redundant in the claims of the '085 patent, which are already limited to crystalline forms.").)

Patent. (See dkt. 49 at 5-8.) He explained that there is no sharp distinction between crystalline and amorphous states:

> A person of ordinary skill in the art would understand that "the magnesium salt of S-omeprazole trihydrate" could be crystalline or amorphous and could have a mixture of crystalline and amorphous features. At the time of the invention, it was well-understood by those skilled in the art that solid state materials are rarely 100% amorphous or 100% crystalline. They exist on what could be described as a continuum, ranging from completely amorphous material exhibiting complete disorder to very crystalline material exhibiting three-dimensional long range order with few ordering defects. Within this continuum, material can exist in an intermediate state or mesophase. Mesophases lack three dimensional long range order but can exhibit X-ray diffraction peaks. There is no definitive dividing line between the crystalline and amorphous states.

(Dkt. 49 at 5.)[95] He asserted that the Haleblian text, cited by defendants' experts, acknowledged this point.[96] He concluded that a POSA would understand that material with

[95] Dr. Atwood disagreed with Dr. Byrn's discussion regarding crystalline and amorphous materials existing on a continuum. (See Mylan action, dkt. 269 at 6-7.) He cautioned that describing a "continuum" is not the same as describing a mixture of crystalline and amorphous solids in a composition of matter. (Id. at 6.) He asserted that the discussion of an "intermediate state" or "mesophase" was out of context – as the POSA would understand mesophase as referring to an intermediate state of matter between liquid and a solid crystal, not an amorphous solid and a solid crystal. (Id. at 7.)

[96] The portion of the Haleblian text Dr. Byrn refers to discusses the differences between X-ray patterns given by amorphous and crystal forms, and is reproduced here:

> The most common amorphous solid is glass. Its atoms are put together in a nonuniform array compared to its crystalline form.
> . . .
> Randall and coworkers (24-28) reported that when a substance is capable of existing in both amorphous and crystalline forms, then the X-ray pattern given by the amorphous form may be regards as a very diffuse version of the crystal pattern. There is, in fact, no sharp distinction between crystalline and amorphous states. If, starting with a coarsely crystalline solid, the size of the crystals could be

less than 100% crystallinity could be covered by claims 1 and 2 of the '085 Patent. (Id. at 5.)

Dr. Byrn disagreed with the other experts that the POSA would have understood the term hydrate to denote a crystalline form. (Id. at 6.) He explained that his prior publications, cited by the other experts on this issue (see n. 113, infra), which admittedly describe hydrates as crystalline, do not state that hydrates can *only* be crystalline. (Id.) He also stated that the specification itself contemplates amorphous hydrates. (Id. at 7.)[97] He further stated that the Khankari text, see n. 116, infra, cited by defendants' experts, reflects the POSA's understanding of the existence of amorphous hydrates and techniques for creating the same. (Id. at 8.)

Dr. Byrn also opined that the POSA would not understand the term "the magnesium salt of S-omeprazole trihydrate" to include any purity limitations, such as

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> reduced by stages and an X-ray diffraction photograph could be taken at each stage, the photographs would become diffuse when the crystal size fell below about 10^{-5} cm. With reduction of crystal size, the reflections become increasingly diffuse until the limit is reached at 10^{-7}–10^{-8} cm, the region of atomic dimensions, where the word crystal, with its implication of precise pattern repetition, ceases to be appropriate.

Haleblian, Characterization of Habits and Crystalline Modifications of Solids and Their Pharmaceutical Applications, 64 J. Pharm. Sci. 6, 1269-88 (1975). (Dkt. 38-2 at 83.)

[97] Dr. Byrn referred to the language found in the '070 Patent at col. 2, ll. 55-62. This language has been the subject of intense disagreement among the experts. For example, Dr. Atwood opined that this language would be understood to reference the existence of an amorphous form of the magnesium salt of S-omeprazole, but not amorphous hydrates. (See Mylan action, dkt. 232-16 at 39-40; dkt. 269-1 at 10-11.)

those proposed by Perrigo or Mylan. (See id. at 8-10.)[98] He repeatedly emphasized the fact that no purity limitations appear in either claim 1 of the '085 Patent or claim 1 of the '070 Patent. Dr. Byrn asserted that the written description discusses three types of purity: chemical purity, enantiomeric purity, and phase purity, which he previously stated described examples or preferred embodiments. (See id.) He stated that the term "substantially pure," as used in the written description, would be understood by the POSA as referring to chemical purity, which he explained "signifies the extent to which the substance is free from detectable impurities or contaminants." (Id. at 9.) He stated that the term "substantially free," as used in the written description, would be understood by the POSA as referring to enantiomeric purity (i.e., "substantially free from magnesium salts of R-omeprazole") and phase purity (i.e., substantially free from other forms of magnesium S-omeprazole"). (Id. at 9-10.) Based on this description, he asserted that the purity limitations proposed by Perrigo (enantiomeric purity and phase purity) and Mylan (chemical purity) were different from each other, injecting further confusion into the

[98] Both Mylan and Perrigo proposed constructions that include a purity limitation. Perrigo's proposed construction requires the "crystals of the magnesium salt of S-omeprazole trihydrate" to be "substantially free from magnesium salts of R-omeprazole and other forms of magnesium salts of S-omeprazole." See nn. 14 and 15, supra and accompanying text. Mylan's proposed construction requires the "crystalline magnesium salt of S-omeprazole having exactly three waters of hydration" to be "substantially pure." See n. 15, supra. Dr. Ruffalo explained that the term "substantially pure," as used in the context of Mylan's proposed construction, is also considered to be "polymorphically pure" S-omeprazole magnesium trihydrate to the extent that no other physical forms are present (i.e. hydrates other than the trihydrate, solvates, amorphous materials, magnesium salts of R-omeprazole and other prior art forms, etc.). (See Mylan action, dkt. 232-18 at 14.)

defendants' proposed constructions. (Id. at 10.)[99] He further opined that the purity language found in the written description was in relation to the process aspects of the patent (e.g., examples 1 and 7), not the compound itself. (Id. at 9.)

ii. "characterized by the following major peaks in its X-ray diffractogram" and "represented by "FIG. 1"

AstraZeneca proposes that the claim term "characterized by the following major peaks in its X-ray diffractogram" be construed as follows: "identifiable by reference to an X-ray diffractogram that includes the major peaks below." (Dkt. 36 at 3.) AstraZeneca proposes that the claim term "represented by FIG. 1" be construed as follows: "represented by Figure 1 of the '070 patent." (Id.)

Dr. Byrn's position was that the claimed compound would be identifiable or distinguishable by the presence of a certain unique X-ray diffraction peak or collection of peaks, without exhibiting every single peak listed in claim 1 of the '085 Patent or shown in Figure 1 of the '070 Patent. The level of sameness between the major listed peaks in claim 1 or Figure 1 required to identify the claimed compound is at the heart of the dispute with respect to these claim terms.

With respect to the term "characterized by the following major peaks in its X-ray diffractogram" in claim 1 of the '085 Patent, Dr. Byrn declared that a POSA would

[99] Dr. Atwood disagreed with this distinction. (See Mylan action, dkt. 269-1 at 12.) He asserted that Mylan's proposed construction would include all three types of purity and that the specification supports this interpretation based on the language "free from." (See id.) Additionally, Dr. Ruffalo's second declaration was devoted almost exclusively to rebutting Dr. Byrn's opinions regarding the term "substantially pure." (See Mylan action, dkt. 247-7.)

understand the term "characterized" to be an inclusive or open-ended term that does not exclude additional, unrecited elements. (Dkt. 40 at 10.)[100] For this reason, he explained that a POSA would understand that the claimed compound would be distinguishable by the presence of the listed major peaks in claim 1 of the '085 Patent, although additional, unrecited peaks may also be present. (Id. at 10-11.) He further declared that a POSA would also understand the term "characterized" to allow for experimental error. He explained that, with experimental error, not every peak listed in claim 1 of the '085 Patent would necessarily be present in every diffractogram. (Id. at 11.) Therefore, the claimed compound would be distinguishable to the POSA by the presence of certain unique peaks or collections of peaks, even if every peak listed in claim 1 is not displayed. (Id. at 11.)

Dr. Byrn explained that a POSA would understand the term "d-value/Å," as it appears in claim 1 of the '085 Patent, to be a measurement indicating the spacing between lattice planes in a crystal ("d-spacings") for the peaks in an X-ray diffractogram. (Id. at 11.) He asserted that the accuracy in the measurement of d-spacings is variable and that one should look for a range of d-spacings when identifying a compound in relation to a reference diffractogram. (Id.) Dr. Byrn also stated that the term "relative

[100] For this definition of "characterized," Dr. Byrn cited section 2111.03 of the 2014 edition of the MANUAL OF PATENT EXAMINING PROCEDURE, which provides an identical definition for that term, as follows: "The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps." (Dkt. 40-16 at 7.) On the other hand, Dr. Atwood opined that the POSA would not be familiar with this reference, but he did not disagree with the notion that "characterized" is an inclusive or open-ended term that does not exclude additional, unrecited elements. (See Mylan action, dkt. 247-6 at 10.)

intensity," as used in the table in claim 1 of the '085 Patent, is understood by a POSA to mean the ratio of the intensity of a peak (i.e., the relevant peak size) with a particular d-value to the intensity of the strongest peak in the diffraction pattern. (Id.) He explained that relative intensities may vary considerably between a sample and a reference of the same substance.[101] Dr. Byrn also indicated that a POSA would understand that the appearance of an X-ray diffractogram could be influenced by multiple factors, such as experimental conditions, that could result in a situation where not every listed peak would be present. (Id. at 11-12.)[102] For these reasons, he concluded that every single peak listed in claim 1 of the '085 Patent would not necessarily need to be present, or present with the listed relative intensity, for the POSA to identify the compound of claim 1 of the '085 Patent. (Id.)

With respect to the term "represented by FIG. 1" in claim 1 of the '070 Patent, Dr. Byrn likewise declared that a POSA would understand the term "represented" to be a flexible term, not requiring exact identity with Figure 1, because X-ray powder diffraction is an experimental technique that is subject to experimental variation and multiple external factors. (Id. at 12.)

[101] Dr. Atwood agreed that relative intensities can vary to some extent. (See Mylan action, dkt. 247-6 at 10.)

[102] Dr. Atwood disagreed with Dr. Byrn on this point. He asserted that experimental error will not cause peaks to be missing from a diffractogram. (See Mylan action, dkt. 247-6 at 10.) Rather, he stated that experimental error means that peak positions will vary to a certain extent, but will not be missing. (Id.)

When discussing the opposing construction positions of the parties for the terms "characterized by the following major peaks in its X-ray diffractogram" and "represented by FIG. 1," Dr. Byrn opined that the phrase "normal experimental error" proposed by the opposing parties was unclear and undefined, and that it may not adequately account for factors that may affect an X-ray diffractogram or how X-ray diffraction is performed and analyzed by a POSA. (Dkt. 49 at 10-11.) Dr. Byrn explained that other materials present in a dosage form or composition may generate obscuring or interfering peaks:

> [W]here a compound is a component of a dosage form or pharmaceutical composition, other materials present in the dosage form or composition, such as crystalline excipients, may generate their own X-ray diffraction peaks, which can obscure or interfere with the peaks of the compound in question. Many common pharmaceutical excipients generate their own X-ray diffraction patterns and will accordingly have this effect. As a result, in a multicomponent system, such as a dosage form or pharmaceutical composition, a [POSA] will consider the X-ray diffractogram as a whole, taking into account interfering peaks from other components when identifying or characterizing a particular compound.

(Id. at 11.)[103] Thus, Dr. Byrn's position is that the construction proposed by AstraZeneca would necessarily account for the experimental error that is inherent in x-ray powder diffraction testing.

[103] Dr. Atwood agreed that other materials present in a dosage form, such as crystalline excipients, may exhibit their own XRPD pattern that may interfere with the recited peaks. (See Mylan action, dkt. 269-1 at 13.) However, he asserted that the POSA would run the individual excipients in order to identify those peaks attributable to the excipients. (Id.)

b. Andrx's expert testimony and exhibits

Dr. Zaworotko was presented by Andrx as an expert in the field of solid state chemistry. His qualifications are summarized in the margin.[104] Dr. Zaworotko's first declaration (dkt. 38-3) includes a thorough recitation of the scientific background pertinent to the claim construction, including discussion of crystalline and amorphous solid forms, solvates and hydrates, characterization of solid state forms, and coordination chemistry of the magnesium salt of S-omeprazole. (See dkt. 38-3 at 10-20.)[105] His second declaration (dkt. 47-2) includes additional background information on the stages of drug discovery and development. (Dkt. 47-2 at 2.) We will provide a brief summary of the scientific background as set forth by Dr. Zaworotko here.

Dr. Zaworotko explained that crystals are a type of solid composed of molecules, atoms, or ions that interact with each other (via chemical bonds) to form an ordered arrangement that repeats in three dimensions. (Dkt. 38-3 at 10.) There are multiple general classes of crystalline solids, including molecular crystals, metallic crystals, ionic crystals and network crystals. (Id. at 11.) Dr. Zaworotko explained that most drug

[104] Dr. Zaworotko has qualifications as a university professor in various positions in the areas of chemistry and crystal engineering. (Dkt. 38-3 at 3-4.) He has published approximately 330 articles and is a named inventor on approximately twenty issued or pending patents, pertaining mostly to crystallization, X-ray crystallography, crystal engineering, crystal packing, polymorphism, and related topics. (Id. at 5.) He has also served as a consultant to various entities within the pharmaceutical community. (Id. at 6.)

[105] Mylan's expert, Dr. Atwood, also provided a thorough recitation of the scientific background, covering topics such as crystallization, polymorphism, solvates and hydrates, amorphous solids, and characterization by X-ray powder diffraction. (See Mylan action, dkt. 232-16 at 10-20.)

substances or active pharmaceutical ingredients ("APIs") are molecular crystals formed from organic molecules and ions. (Id.) The arrangement of molecules defines a given crystal form. The "unit cell" is the basic building block of a crystalline solid. (Id.) Dr. Zaworotko also explained that a solid can assume an amorphous form, which he describes as "not crystalline." (Id.) He explained that amorphous solids do not have a "unit cell," are composed of randomly oriented molecules, ions, or atoms with no long-range order, and are less stable than a crystalline form of the same compound. (Id. at 11-12.)

Dr. Zaworotko stated that compounds existing in more than one crystal structure are "polymorphic," which means the compound can crystallize into more than one distinct crystal structure through different crystal packing motifs. (Id. at 12-13.)

Dr. Zaworotko defined a "solvate" as a compound that "crystallizes from solution into a crystalline solid that traps solvent molecules within the crystal lattice." (Id. at 13.) He explained that solvates can be stoichiometric (having a fixed ratio of solvent to compound) or non-stoichiometric (having a variable ratio of solvent to compound). (Id.) If the solvent is water, the crystalline solid is known as a "hydrate." (Id.)

Dr. Zaworotko stated that in the field of solid state chemistry, a hydrate cannot be amorphous. He explained that in a stoichiometric hydrate, water trapped in the crystal lattice can contribute to the dimensions of the resulting "unit cell," and that there may be different stoichiometric hydrates of the same compound. (Id. at 14-15.) On this point, he stated that prior to 1997, a standardized nomenclature of stoichiometric hydrates existed. (Id. at 14-15.) Dr. Zaworotko explained that a hydrate with one water of crystallization

for every two host molecules was known as a "hemihydrate." (Id. at 14.) A hydrate with one water of crystallization for each host molecule was known as a "monohydrate." (Id. at 15.) A hydrate with two waters of crystallization for each host molecule was known as a "dihydrate." (Id.) A hydrate with three waters of crystallization for each host molecule was known as a "trihydrate." (Id.) He also explained that solvates and hydrates may be polymorphic, which he defined as having "different unit cell dimensions and/or packing motifs . . . even though the ratio of solvent or water in the lattice to host is the same in each polymorph." (Id. at 15.)

With respect to the characterization of solid state forms, Dr. Zaworotko explained that numerous methods, such as single crystal X-ray diffraction (SCXRD) and X-ray powder diffraction ("XRPD") are known to identify crystals and determine attributes of a crystal structure. Dr. Zaworotko described XRPD as the "gold standard" for identification of the crystal form of an API, since it can produce a pattern of peaks that act as a signature for a particular crystalline form. (Id. at 16.) He explained that with XRPD, X-rays are directed at the sample (which he stated may be a "bulk crystalline" or "microcrystalline" sample) at varying angles, and that if the sample is crystalline, it will diffract X-rays at specific angles due to its crystalline structure, providing a unique pattern of peaks. (Id.) He also noted that sample-specific factors may influence readings, and that XRPD is subject to some experimental error. (Id. at 17.) He further explained that amorphous materials do not diffract X-rays at specific angles, and instead scatter X-rays to create a diffuse pattern. (See id. at 17-18.)

Dr. Zaworotko explained that the magnesium salt of S-omeprazole belongs to a class of compounds known as coordination compounds, which are compounds comprised of metal cations bonded with one or more molecules or ions called ligands. (Id. at 18.) The geometry of coordination compounds enables a phenomenon known as structural isomerism in which molecules with an identical chemical formula have bonded together in different orders. (See id. at 19.) Dr. Zaworotko explained that structural isomers with differing structures (but the same chemical formula) exhibit different crystal structures and properties. (Id.) He concluded that S-omeprazole anions and water molecules can coordinate to magnesium cations in multiple modes and geometric arrangements due to structural isomerism. (Id. at 20.)

In his second declaration, Dr. Zaworotko explained that the drug discovery and development process generally takes place in three distinct stages: a "molecules" stage, a "materials" stage, and a "medicines" stage. He stated that the education and training of a POSA and the nomenclature in each stage was not always consistent; thus, distinguishing among these stages is important. (Dkt. 47-2 at 2.) He describes the "molecules" stage as including "medicinal chemistry for the discovery of new chemical entities along with biological and pharmacological screening activity." (Id.) He describes the "materials" stage as the pre-formulation stage as including "discovery of a drug substance . . . suitable for use as a material in a drug product." (Id.) He describes the "medicines" stage as the formulation stage which includes the combining of the drug substance with inactive ingredients, excipients in order to form the drug product. (Id.) He stated that the

'085 and '070 Patents relate to the "materials" stage of drug discovery and development, and that it is important to consider the '085 and '070 Patents in that context. (Id.)

i. "The magnesium salt of S-omeprazole trihydrate"

To review, Andrx proposes that the claim term "the magnesium salt of S-omeprazole trihydrate" be construed as follows: "the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole." (Dkt. 36 at 3.) Dr. Zaworotko opined that the POSA would have understood the term "the magnesium salt of S-omeprazole trihydrate" to refer to "the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole," which he stated was the plain and ordinary meaning to a POSA at the time of the invention. (Dkt. 38-3 at 21.) He explained that the term "trihydrate" refers to a crystalline form that has three water molecules, entrapped in its crystal lattice, for every molecule of compound. (Id.) With respect to the three water molecules, he declared that:

> [t]he POSA referred to those water molecules as "waters of crystallization" or "waters of hydration." The POSA understood that the term "trihydrate" refers to a stoichiometric hydrate and thus that the waters of crystallization in the claimed trihydrate contribute to the dimensions of the unit cell. The POSA thus understood that waters of crystallization contribute to the structure unique to the hydrate (or the particular polymorph of the hydrate). Thus, the POSA understood that waters of crystallization were the waters that define the hydration level (*e.g.*, mono-, di-, tri-, etc.) of hydrate.

(Id. at 22.)[106]

Looking at the intrinsic evidence for the '085 and '070 Patents, Dr. Zaworotko stated that both the written description and the prosecution histories of the '085 and '070 Patents support his opinion that the claimed trihydrate is crystalline. In his opinion, statements made in the written description indicate that the trihydrate is crystalline and were used to distinguish it from the prior art on that basis. (Id. at 22-23.)[107] Other statements, he noted, are premised on the trihydrate being crystalline. He pointed to the discussion of XRPD and the unit cell at column 2, lines 43-51 and 63-64 of the '070 Patent. (Id. at 22-23.)

Further, he stated that the methods of making the trihydrate in Examples 1 and 7 would indicate to the POSA that the resulting trihydrate is crystalline. (Id. at 23.)[108] He explained that Examples 1 and 7 involve crystallization from water followed by drying

[106] Dr. Zaworotko also stated that the construction offered by Perrigo and Mylan for this term were consistent with Andrx's proposed construction, as all three require the hydrate to be crystalline. (Id. at 26.) Mylan's experts, Dr. Atwood and Dr. Ruffalo described the magnesium salt of S-omeprazole as crystalline slightly differently as "having exactly three waters of hydration." (See Mylan action, dkt. 232-16 at 38; dkt. 232-18 at 14.)

[107] For example, he pointed to the statement at column 2, lines 51-53 of the '070 Patent: "[t]he compound of the invention is characterized by being highly crystalline, i.e., having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art." (Dkt. 38-3 at 22-23.)

[108] Dr. Ruffalo and Dr. Atwood agree that Examples 1 and 7 indicate to the POSA that the resulting trihydrate is crystalline and none of the examples teach a process for making an amorphous form of S-omeprazole magnesium trihydrate. (See Mylan action dkt. 232-18 at 17-18; dkt. 232-16 at 40-41.)

under vacuum, a process intended to remove excess water, which he describes as "water that is not integrated into the unit cell." (Id.)

With respect to the prosecution history, Dr. Zaworotko opined that a POSA would understand many of the Applicants' arguments made in response to Office action rejections to be premised on the concept that the claimed trihydrate is crystalline. Specifically, Dr. Zaworotko pointed to statements describing the invention made in response to the November 27, 2000 Office action during the prosecution of the '085 Patent and in response to the April 29, 2005 Office action during the prosecution of the '070 Patent. (Id. at 24.)[109,110] Dr. Zaworotko also highlighted the Applicants' discussion of "guest" molecules in their response to the November 27, 2000 Office action as evidencing an understanding by the Applicants that the waters in a trihydrate must be waters of crystallization. (Id.) He explained that the Applicants argued it was unpredictable to add water as a guest molecule in response to the examiner's assertion that it was known that organic solid material may include "guest" molecules for the purpose of forming crystals. (Id.)

Looking at the extrinsic evidence, Dr. Zaworotko stated that in the field of solid state chemistry, hydrates were long recognized as crystalline forms defined by the number of waters of crystallization they contain in their crystal lattice. On this point, he

[109] See Section II.B.1, supra.

[110] Dr. Atwood and Dr. Ruffalo agreed and referred to the same statements as well as others on this point. (See Mylan action, dkt. 232-16 at 42-46l dkt. 232-18 at 20-30.)

referred to several texts.[111] Two of these texts were authored by plaintiff's expert, Dr. Byrn. See n. 111, supra.[112] In Dr. Zaworotko's opinion, Dr. Byrn's prior writings distinguished solvates and hydrates from amorphous forms on the basis of crystallinity.[113]

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[111] Dr. Zaworotko cited these texts as supporting the statement that hydrates were known in the art to be crystalline forms defined by the number of waters of crystallization: Brittain, Methods for the Characterization of Polymorphs and Solvates, in Polymorphism in Pharmaceutical Solids, Vol. 95 (Marcel Dekker, New York 1999) ("Brittain") (dkt. 38-2 at 2-54); Byrn, et al., Solid-State Pharmaceutical Chemistry, Chem. Mater. 1994, 6, 1148-58 (1994) ("Byrn 1994") (dkt. 38-2 at 56-66); Byrn et al., Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations, Pharm. Res. Vol. 12, No. 7, 945-54 (1995) ("Byrn 1995") (dkt. 38-2 at 68-78); Haleblian, Characterization of Habits and Crystalline Modifications of Solids and Their Pharmaceutical Applications, 64 J. Pharm. Sci. 6, 1269-88 (1975) ("Haleblian") (dkt. 38-2 at 80-99); Khankari & Grant, Pharmaceutical hydrates, Thermochimica Acta, 248 (1995) ("Khankari") (dkt. 38-2 at 101-116); and Wells, Structural Inorganic Chemistry (3d 1962) ("Wells") (dkt. 38-2 at 118-120).

[112] Dr. Atwood also cited the Byrn 1995 reference, the Haleblian reference, and a third reference, Byrn, Solid-State Chemistry of Drugs, Academic Press (1982) (Mylan action, dkt. 232-7), to demonstrate the understanding of the term "hydrate" and "solvate" to a POSA.

[113] The Byrn 1994 article states:

> The most common solid forms that may be found for a given drug substance are as follows: **crystalline polymorphs**, forms having the same chemical composition but different crystal structure and therefore different densities, melting points, solubilities, and many other important properties; **solvates**, forms containing solvent molecules within the crystal structure, giving rise to unique differences in solubility, response to atmospheric moisture, loss of solvent, etc. Sometimes a drug product may be a **desolvated solvate**, formed when solvent is removed from a specific solvate while the crystal structure is essentially retained—again, many important properties are unique to such a form; finally, **amorphous** solid forms that have no long-range molecular order (i.e., no crystallinity) and which tend to be more soluble, more prone to moisture uptake, and less chemically stable than their crystalline counterparts (pharmaceutical processing operations may produce solids of low crystallinity intermediate between that of a crystalline solid and an amorphous solid).

Byrn, et al., Solid-State Pharmaceutical Chemistry, Chem. Mater. 1994, 6, 1148-58 (1994). (Dkt. 38-2 at 56 (emphasis in original).)

The Byrn 1995 article states:

> Polymorphs exist when the drug substance crystallizes in different crystal packing arrangements all of which have the same elemental composition (Note that hydrates can exist in polymorphs). Hydrates exist when the drug substance incorporates water in the crystal lattice in either stoichiometric or non-stoichiometric amounts. Desolvated solvates are produced when a solvate is desolvated (either knowingly or unknowingly) and the crystal retains the structure of the solvate. Amorphous forms exist when a solid with no long range order and thus no crystallinity is produced.

Byrn et al., Pharmaceutical Solids: A Strategic Approach to Regulatory Considerations, Pharm. Res. Vol. 12, No. 7, 945-54 (1995). (Dkt. 38-2 at 69.)

He further stated that the additional cited literature on the subject, namely Britain,[114] Haleblian,[115] Khankari,[116] and Wells,[117] also reflect hydrates being known in the art as crystalline forms. (Id. at 25.)

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[114] The Brittain text states:

> Compounds may be *polymorphs* (forms having the same chemical composition but different crystal structures), *solvates* (forms containing solvent molecules within the crystal structure, *desolvated solvates* (forms when the solvent is removed from a specific solvate while still retaining the original crystal structure), or *amorphous* (solid forms that have no long-range molecular order).

Brittain, Methods for the Characterization of Polymorphs and Solvates, in Polymorphism in Pharmaceutical Solids, Vol. 95 (Marcel Dekker, New York 1999). (Dkt. 38-2 at 4 (italics in original).)

[115] The Haleblian text states: "Solvates are molecular complexes that have incorporated the crystallizing solvent molecule in their lattice. When the solvent incorporated in the solvate is water, it is called a hydrate." Haleblian, Characterization of Habits and Crystalline Modifications of Solids and Their Pharmaceutical Applications, 64 J. Pharm. Sci. 6, 1269-88 (1975). (Dkt. 38-2 at 87.)

[116] The Khankari text states:

> With some crystalline solids, solvent in the surrounding medium may become incorporated into the crystal lattice of the compound in stoichiometric proportions. These molecular adducts are termed solvates. Hydrates are formed when water is the solvent of crystallization. In hydrates water occupies definite positions in the crystal lattice, usually by forming hydrogen bond(s) and/or coordinate covalent bond(s) with the anhydrate drug molecules.

Khankari & Grant, Pharmaceutical hydrates, Thermochimica Acta, 248 (1995). (Dkt. 38-2 at 102.)

[117]The Wells text states:

> One of the simplest ways of purifying a compound is to recrystallize it from a suitable solvent. The crystals separating from the solution may consist of the pure compound or they may contain 'solvent of crystallization'. For most salts water is a convenient solvent, so that crystals containing water—hydrates—have been known from the earliest days of chemistry, and many inorganic compounds are normally obtained as hydrates.

Dr. Zaworotko disagreed with many points and issues raised by Dr. Byrn. First, he disagreed with Dr. Byrn that a POSA would interpret the written description as acknowledging the existence of an amorphous hydrate. (Dkt. 47-2 at 3.)[118] His interpretation of this portion of the written description was that the inventors were distinguishing their invention from prior art forms, which included an amorphous form – not that hydrates or solvates were or could be amorphous. (Id.)[119]

As noted in Section II.B.3.a, supra, Dr. Zaworotko challenged Dr. Byrn's reliance on four post-priority date references (see n. 89, supra) for the proposition that the existence of amorphous hydrates were well known by POSAs at the relevant time. In addition to challenging the references based on their post-priority date status, Dr. Zaworotko challenged them substantively. Specifically, Dr. Zaworotko opined that Megarry (2011), appeared to be the first reported instance of using a process called cryomilling to obtain an amorphous hydrate. (Id. at 4.) However, he noted that Megarry (2011) did not relate to S-omeprazole magnesium, and that it is unknown how S-omeprazole magnesium responds to cryomilling. (Id. at 4, 10.) He explained that the '634 Patent does not discuss a stoichiometric hydrate or suggest a stoichiometric hydrate could be amorphous, and that its disclosure was not sufficient to allow a POSA to

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Wells, Structural Inorganic Chemistry (3d 1962). (Dkt. 38-2 at 120.)

[118] Specifically, Dr. Zaworotko refers to the language found in the '070 Patent at col. 2, ll. 55-62, that as noted supra has been the subject of intense disagreement among the experts.

[119] Dr. Atwood and Dr. Ruffalo have similar positions regarding this portion of the written description. (See Mylan action, dkt. 232-16 at 39; dkt. 232-18 at 16.)

conclude a hydrate was obtained, noting the '634 Patent failed to report on measured moisture content. (Id.) He explained that the '842 Patent relates to cephalosporin, not S-omeprazole. (Id.) He stated that the examples purporting to describe an amorphous hydrate of cephalosporin failed to explain how water content was measured and did not provide sufficient information to determine whether water was absorbed into the crystal lattice as water of crystallization or by adhering to the surface of the solid. (Id.) With respect to WO2004/020436, Dr. Zaworotko opined that it fails to provide sufficient information for a POSA to conclude that an amorphous hydrate was obtained or even possible because it was not clear whether water is absorbed into the crystal lattice or simply adheres to the surface of the solid described in that reference. (Id. at 6.)

In addition, and as noted in Section II.B.3.a, supra, Dr. Zaworotko also took issue with Dr. Byrn's reliance on the six additional references (see n. 90, supra) offered in Dr. Byrn's second declaration for the same proposition, that amorphous hydrates were known and discussed in the literature at the relevant time. (See dkt. 54-1.) Dr. Zaworotko opined that these references were irrelevant to the scientific field to which the '085 and '070 Patents pertain, i.e., the discovery of solid forms of drug substances suitable for use in drug products, namely Type A molecular solids. (See id. at 2.)[120] Dr. Zaworotko explained that there are four distinct categories of solid substances: molecular solids, ionic solids, metallic solids, and network solids. (Id. at 2.) He further explained that

[120] Dr. Atwood also took issue with these additional references, asserting that each was irrelevant to the field to which the '085 and '070 Patents pertain. (See Mylan action, dkt. 269-1 at 8-10.)

there are two types of molecular solids, Type A[121] and Type B,[122] and that solid forms of drug substances are Type A molecular solids. (Id.) He stated that this was important because the nomenclature for molecular solids, and specifically the term "hydrate," is not necessarily interchangeable among the four classes of solid substances, or even between Type A and Type B molecular solids. (Id. at 4.) He reviewed each of the six additional references and concluded that they referred to Type B molecular solids (i.e., polymers or nanoparticles) or network solids, not Type A molecular solids. (Id.) For this reason, he concluded that each of the six additional references were not relevant to the '085 or '070 Patents. (See id. at 4-6.)

Dr. Zaworotko also disagreed with Dr. Byrn's articulation of what constitutes a hydrate, stating that Dr. Byrn's definition, characterizing a hydrate as having "some structure that can bind water in a regular way," is overbroad, unsupported, and in conflict with Dr. Byrn's own publications both before and after the priority dates of the '085 and

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[121] Dr. Zaworotko provided the following description of Type A molecular solids:

> Type A [molecular solids] occur when the compound that forms a molecular solid is relatively pure and of small or medium molecular weight. Type A [molecular solids] tend to be homogeneous and crystalline, as crystalline solids are energetically favored. Almost all organic molecules, organic salts and coordination complexes exist as Type A molecular solids.

(Dkt. 54-1 at 3.)

[122] Dr. Zaworotko provided the following description of Type B molecular solids: "Type B [molecular solids] occur when the compound forming a molecular solid is impure with high molecular weight, such as a polymer. Type B tend to be amorphous. Polymers or nanoparticles, containing an array of different sized molecules or particles, tend to form Type B molecular solids." (Dkt. 54-1 at 3.)

'070 Patents. (Id. at 6.) He stated that any implication that the magnesium salt of S-omeprazole can form a hydrophilic layer that incorporates water molecules is speculative and not a typical feature for such compounds. (Id. at 7.) Dr. Zaworotko also stated that Dr. Byrn's overbroad definition of the term "trihydrate" conflicts with the International Union of Pure and Applied Chemistry's ("IUPAC") Principles of Chemical Nomenclature because it would include aqua complexes,[123] i.e., compounds in which none of the three waters are absorbed into the crystal lattice, but instead are all in coordination bond with the magnesium ion. (See id. at 7-9.) Dr. Zaworotko similarly found the dictionary definitions for the term "trihydrate" cited by Dr. Byrn (see n. 91, supra) to be overly broad and inapposite to the field of the patents-in-suit. (Dkt. 47-2 at 9-10.)

Finally, Dr. Zaworotko clarified the scope of Andrx's proposed construction. He explained that it would not limit claim 1 of the '070 Patent to a particular polymorphic form, and would in fact "cover all crystalline polymorphs of S-omeprazole magnesium trihydrate, and thus, be broader than claim 1 of the '085 patent, which is limited to a particular crystalline polymorph of that trihydrate." (Id. at 11.)[124]

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[123] In coordination nomenclature, a coordination entity is composed of a central atom or atoms to which are attached other atoms or groups of atoms, which are termed ligands. Leigh, Principles of Nomenclature: A Guide to IUPAC Recommendations (1998) ("Leigh") (dkt. 47-1 at 173.) The number of central atoms in a single coordination entity is denoted by the nuclearity: mononuclear, dinuclear, trinucleaer, etc. (Id. at 175.) For mononuclear coordination compounds, the central atom is listed first, followed by the formally anionic ligands, neutral ligands, and polydentate ligands. (Id. at 176.) Water molecules as ligands take the name aqua. (Id. at 177.)

[124] Dr. Ruffolo provided a similar argument with respect to claim 1 and 2 of the '070 Patent. He stated that claim 1 of the '070 patent would encompass all crystalline forms of S-

ii. "characterized by the following major peaks in its X-ray diffractogram" and "represented by "FIG. 1"

Andrx proposes that the claim term "characterized by the following major peaks in its X-ray diffractogram" be construed as follows: "exhibiting, within the range of normal experimental error, each of the following as major peaks in its X-ray diffractogram, each such peak falling within the range for relative intensity recited for that peak such ranges being defined at Column 5, lines 29-39 [of the '085 Patent]." (Dkt. 36 at 3.) Andrx proposes that the claim term "represented by FIG. 1" be construed as follows: "exhibiting an x-ray powder diffractogram that is the same as Figure 1 of the '070 patent within normal experimental error." (Id.)

As noted above, the level of sameness between the major listed peaks in claim 1 of the '085 Patent or Figure 1 of the '070 Patent required to identify the claimed compound is at the heart of the dispute with respect to these claim terms. Dr. Zaworotko advocated for constructions that would require all of the peaks to be present and explicitly account for experimental error.

With respect to the claim term "characterized by the following major peaks in its X-ray diffractogram" of claim 1 of the '085 Patent, Dr. Zaworotko's position was that this term should be construed "to require all 13 peaks recited in the table set forth in the claim, including their respective relative intensities, within normal experimental error." (Dkt. 38-3 at 27.) He declared that the POSA would understand that claim 1 of the '085

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omeprazole magnesium trihydrate, and that claim 2 defines a specific crystalline structure that was characterized using XRPD. (See Mylan action, dkt 232-18 at 31.)

Patent is directed to a particular trihydrate that, when analyzed using XRPD, would exhibit the 13 peaks recited in the table, and that those peaks must fall into the specified relative intensity ranges. (Id. at 28.) He explained that a POSA looking to identify (or distinguish) one sample from another or looking to compare the XRPD of a sample to a reference XRPD would compare the pattern in its entirety, and not focus on matching or mismatching one peak, or even several peaks to the exclusion of others. (Id. at 28.) He further opined that the POSA would understand the pattern of claim 1 of the '085 Patent to be compared as the set of 13 peaks, each with a relative intensity value falling into a particular recited range due to the '085 Patent's presentation of the 13 peaks as intensity ranges, rather than particular numerical values. (Id. at 28-29.)[125]

Dr. Zaworotko disagreed with Dr. Byrn that claim 1 of the '085 Patent could be construed as requiring fewer than all recited peaks. (See id. at 29.) Turning to the written description, he declared that the POSA would not interpret the statement found at the conclusion of Exhibit 7, "[t]he product was analyzed using X-ray powder diffraction and the result complied with FIG.1 and Table 1" (see '070 Pat., col. 9, ll. 48-50), to allow for such imprecision. (Id.) In his opinion, the POSA would conclude the XRPD data for the product of Example 7 was similar enough to the data for Example 1, with respect to all the major peaks and relative intensities of those peaks. (Id.)

[125] The explanatory note to the table shown in claim 1 of the '085 Patent does translate those verbal intensity ranges into numerical ranges, but not precise numbers, e.g., vs (very strong) is 25-100% relative intensity. (See '085 Pat., col. 5 ll. 33-39.)

Dr. Zaworotko also stated that the POSA would understand that XRPD is subject to some experimental error, which would be accounted for by a POSA in any comparison of XRPD diffractograms or data sets. (Id. at 17-18, 29-30.) However, he did not define experimental error, describe the nature of its effect on an XRPD, or how it would be accounted for.

With respect to the term "represented by FIG. 1," Dr. Zaworotko declared that the POSA would understand that term to mean that "the claimed trihydrate exhibits the same [XRPD] as Figure 1, taking into account normal experimental error." (Id. at 30.) He explained that the POSA would subject a given crystal form to XRPD analysis and compare the resulting patterns to determine whether that crystal form is "represented by" Figure 1. (Id.) He again discounted the "complies with" language found in Example 7, stating it should not be viewed as broadening the term "represented by" beyond the construction proposed by Andrx. (Id. at 31.)

c. Perrigo's expert testimony and exhibits

Dr. Buckton was presented by Perrigo as an expert in the field of pharmaceutical research and development including selection and characterization of physical forms, formulation development, pharmaceutical processing and drug delivery systems. His qualifications are summarized in the margin.[126]

[126] Dr. Buckton has qualifications as a university professor in various positions in the area of pharmaceutics. (Dkt. 44-1 at 2-3.) He has also published more than 180 publications. (Id. at 3.)

Like Dr. Zaworotko, Dr. Buckton provided a thorough recitation of the scientific background pertinent to the claim construction in his first declaration.[127] Dr. Buckton's explanations were in accord with those provided by Dr. Zaworotko (see Section II.B.3.b, supra), so there is no need for the Court to repeat them at length here. The Court notes that Dr. Buckton offered explanations for the following concepts and topics: the characteristics and properties of crystalline and non-crystalline (or amorphous) materials, polymorphism, stoichiometric hydrates, and X-ray powder diffraction.

i. "The magnesium salt of S-omeprazole trihydrate"

` Perrigo proposes that the claim term "the magnesium salt of S-omeprazole trihydrate" be construed as follows: "crystals of the magnesium salt of S-omeprazole trihydrate, substantially free from magnesium salts of R-omeprazole and other forms of magnesium salts of S-omeprazole." (Dkt. 36 at 3.)

Dr. Buckton declared that a POSA would understand the term "the magnesium salt of S-omeprazole trihydrate" to mean:

> crystals of S-omeprazole magnesium trihydrate in the context of a bulk product, and that the bulk product is substantially free from: magnesium salts of R-omeprazole, and other physical forms of magnesium salts of S-omeprazole, such as the corresponding magnesium salt compounds described in prior art, which include dihydrates used in the preparation of the trihydrate, and other forms such as anhydrates, hydrates, solvates, and polymorphs or amorphous forms thereof disclosed in the prior art, such as monohydrates, dihydrates,

[127] (See Perrigo action, dkt. 44-1 at 6-11.)

> sesquihydrates, trihydrates, and alcoholates (e.g., methanolates and ethanolates).[128]

Dr. Buckton's opinion is based exclusively on intrinsic evidence, i.e., the written description and the prosecution histories of the '085 and '070 Patents. Dr. Buckton did not cite to any scientific literature in his opinion.

As noted above, Dr. Buckton agreed with Dr. Zaworotko that the term "the magnesium salt of S-omeprazole trihydrate" would be understood by a POSA as limited to a crystalline form. Dr. Buckton stated he was not aware of any publication characterizing a hydrate as amorphous at the time of the invention.[129] However, and as discussed in more detail below, Dr. Buckton's proposed construction included additional limitations that relied on the magnesium salt of S-omeprazole trihydrate being in "bulk product" form.[130] He stated that the Applicants limited "the magnesium salt of S-omeprazole trihydrate" to products for which the S-omeprazole magnesium at the bulk level is trihydrate, "substantially free" of other forms. He explained that it is necessary to consider the entirety of S-omeprazole magnesium present in a product to determine whether that product is (or contains) the claimed magnesium salt of S-omeprazole trihydrate:

> [I]f the entirety of S-omeprazole magnesium for a given product were to consist of trihydrate crystals plus an

[128] (Perrigo action, dkt. 44-1 at 13-15.)

[129] (Perrigo action, dkt. 50-1 at 10-11).

[130] At his deposition, Dr. Buckton admitted that the term "bulk product" does not appear in the claims or the written description. (Perrigo action, dkt. 51-3 at 4-5.)

> insubstantial quantity of another form or forms (e.g., dihydrate, amorphous, etc.), the S-omeprazole magnesium would be "the magnesium salt of S-omeprazole trihydrate" as claimed in the patents. On the other hand, if the entirety of S-omeprazole magnesium for a given product were to consist of trihydrate crystals plus a substantial quantity of another form or forms (e.g., dihydrate, amorphous, etc.), the S-omeprazole magnesium would not be "the magnesium salt of S-omeprazole trihydrate."[131]

Dr. Buckton stated that his position was supported by the intrinsic evidence. He pointed to the written description, which he opined makes clear to the POSA that "the magnesium salt of S-omeprazole trihydrate" refers to the entirety of a bulk product in solid form, in which substantially all of the S-omeprazole magnesium exists in the trihydrate form, not another solid form or forms, such as anhydrous, amorphous, dihydrate, etc.[132] Dr. Buckton explained that, in his opinion, the "substantially free" language found in the written description is meaningful only in the context of a bulk product.[133] He stated that additional statements, such as the invention being "substantially pure," "exist[ing] in a well-defined state," and being "easily distinguishable from any other crystal form of the magnesium salt of S-omeprazole disclosed in the prior art" are further evidence that the term refers to a bulk product.[134] He went on to opine that the stated advantages of the invention, i.e., "being more stable,"

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[131] (Perrigo action, dkt. 44-1 at 17.)

[132] (Id. at 15.)

[133] (Id.)

[134] (Id. at 15-16.)

"easier to characterize," "easier to handle and store," etc., would be understood by the POSA as referring to a bulk product.[135]

At his deposition, Dr. Buckton was asked to define the bounds of the term "substantially free." He could not, and refused to quantify exactly where the term "substantially free" begins and ends.[136] He simply used substitutes for the term "substantially free," describing the amount as "the vast majority" or "majority." See e.g., n. 136. Dr. Buckton disagreed with Dr. Byrn that the "substantially free" language found

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[135] (Id. at 16.)

[136] Dr. Buckton was asked, in a deposition excerpt filed by both AstraZeneca and Perrigo, what the term "is substantially free from" meant, as used in paragraph 44 of his first Declaration. He replied:

> Substantially free means the vast majority of the omeprazole in say the tablet, if that's what we're looking at, the vast majority of it is present as the magnesium salt of S-omeprazole trihydrate. There conceptionally could be some other form there but that would be in the minority, and that's what I'm taking as the meaning now. Whether that is a definite term that you could decide on, we can talk about, but that's what I'm taking as now.

(Perrigo action, dkt. 50-3 at 11-12.) He was then asked if the term "substantially free from" would be satisfied by a material that contains 51 percent of S-omeprazole magnesium trihydrate and 49 percent of something else. In response, he refused to provide a specific cut off quantity:

> I don't have a number so I can't go one by one by one along the way to get to a number. But what I could tell you categorically is if the S-omeprazole trihydrate is in the minority and is a very small part of what is present there, it cannot be that the total S-omeprazole in that product is S-omeprazole trihydrate.

(Id. at 12.) When asked why he could not give an exact number, Dr. Buckton explained that he did not know if the term was definite to determine "whether you're in it or not." (Id.) Dr. Buckton also did not believe the POSA would be able to determine an exact number. (See Id. at 13-14.)

in the written description referred only to examples or embodiments of the invention.[137] He declared that the POSA would understand the nature of the "substantially free" language as limiting based on the written description and prosecution history.[138]

With respect to the written description, Dr. Buckton again pointed to the language found at column 2 of the '070 Patent, and asserted that the characteristics and advantages of the "compound of the invention," always applied to the trihydrate form and would be consistent with the description of a bulk product substantially free of R-omeprazole magnesium and other forms of S-omeprazole magnesium.[139] He explained that the stated characteristics and advantages would not be realized in a product that was dominated by a mixture of R-omeprazole magnesium or other forms of S-omeprazole magnesium.[140]

With respect to the prosecution history, Dr. Buckton relied on the November 27, 2000 Office action and the response thereto in the '085 Patent's prosecution history.[141] Dr. Buckton viewed the examiner's statements and rejection of originally filed claim 1 of '719 Application in the November 27, 2000 Office action as concluding that S-omeprazole magnesium in the prior art contained at least some trihydrate.[142] Thus, he

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[137] (Perrigo action, dkt. 50-1 at 3)

[138] (Id. at 4.)

[139] (Id. at 4-5, 7-9.)

[140] (Id. at 9.)

[141] (See id.)

[142] (See id. at 5.)

viewed the Applicants' response and the Langkilde Declaration as an attempt to distinguish the invention from the prior art by arguing the claimed trihydrate form was substantially free of R-omeprazole and other prior art forms of S-omeprazole magnesium.[143]

Dr. Buckton also disagreed with the claim differentiation arguments put forth by plaintiff. He stated that any differences between claims would not change the POSA's understanding that "the magnesium salt of S-omeprazole trihydrate" is limited to a bulk product substantially free of R-omeprazole magnesium and other forms of S-omeprazole magnesium.[144] With respect to the "highly crystalline form" limitation in claim 2 of the '085 Patent, he reasoned that all material covered by claim 1 and 2 of the '085 is necessarily "highly crystalline" according to the written description.[145, 146]

[143] (See id. at 5-6.)

[144] (Id. at 10.)

[145] (Id.)

[146] Dr. Atwood's view differed on this point to some degree. In his opinion, the POSA would understand that claim 1 of the '085 patent must be crystalline because it exhibits the recited peaks as a result of its long range order. (See Mylan action, dkt. 269-1 at 3-5.) The difference between the claims, he stated, was that claim 2 limits the crystalline forms in claim 1 to those with a "higher degree of long range order." (Id. at 4.) He explained that the degree of long range order in a crystalline solid reveals itself in the XRPD pattern by the sharpness of the peaks. (Id.) Thus, he concluded that claim 2 would exhibit the same peaks as claim 1, but those peaks would appear to be sharper due to the greater degree of long range order, i.e., higher crystallinity. (Id. at 4-5.)

ii. "characterized by the following major peaks in its X-ray diffractogram" and "represented by FIG. 1"

Perrigo proposes that the claim term "characterized by the following major peaks in its X-ray diffractogram" be construed as follows: "having each of the referenced major peaks in its X-ray powder diffractogram within normal experimental error." (Dkt. 36 at 3.) Andrx proposes that the claim term "represented by FIG. 1" be construed as follows: "exhibiting an x-ray powder diffractogram that is the same as Figure 1 of the '070 patent within normal experimental error." (Id.)

Dr. Buckton opined that the claim term "characterized by the following major peaks in its X-ray diffractogram" means that "the product in question exhibits all of the referenced major peaks in its powder X-ray diffractogram within normal experimental error."[147,148] Dr. Buckton opined that the claim term "represented by FIG. 1" means that "the product in question exhibits the same powder X-ray diffractogram shown in Figure 1 within normal experimental error."[149,150]

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[147] (Perrigo action, dkt. 44-1 at 18.)

[148] Mylan's construction for this term was similar to Perrigo's, in that Mylan's proposed construction required each peak to be present, within normal experimental error. Mylan's experts, Dr. Atwood and Dr. Ruffalo, asserted such a construction was supported by the intrinsic evidence (i.e., the context of the claims, statements found in the written description, and statements made during the prosecution history of the '085 Patent) as well as extrinsic evidence (i.e., the use of XRPD to characterize crystalline solid states in the prior art, and prior uses of the word "characterized" in this context.) (See dkt. 232-16 at 53-56; dkt. 232-18, at 35-36.) Dr. Atwood also described AstraZeneca's proposed construction for this term as "incomplete," asserting it does not require the compound to be characterized by XRPD. (See dkt. 232-16 at 56-57.)

[149] (Id.)

[150] Mylan's construction for this term was almost identical to Perrigo's, in that Mylan's proposed construction required the X-ray powder diffraction pattern of the claimed compound to

Dr. Buckton explained at his deposition that "normal experimental error" in the context of his proposed construction means a shift in the positions of peaks, which may be caused by different instruments.[151] He further explained that there may be variation in peak intensity between different samples analyzed by the instrument, and that it was possible for weak peaks to be absent as a result of experimental error, concepts he described as being understood by a POSA.[152]

4. Court findings and claim constructions

a. "the magnesium salt of S-omeprazole trihydrate"

The Court has considered the parties' respective arguments, the patent claims, the specification, the prosecution history, and the relevant extrinsic evidence. The Court adopts Andrx's proposed construction and construes the claim term "the magnesium salt of S-omeprazole trihydrate" as used in the specified claims of the '085 and '070 Patents, to mean "the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole."

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be the same as Figure 1 of the '070 Patent. Mylan's experts asserted such a construction was supported by the intrinsic evidence (i.e., statements found in the written description and the specificity used in the Langkilde Declaration when describing a comparison to the X-ray diffractogram) and the extrinsic evidence discussed in the footnote immediately above. (See dkt. 232-16 at 58-60; dkt. 232-18 at 36-37.)

[151] (Perrigo action, dkt. 50-3 at 16.)

[152] (See id. at 17-18.)

In arriving at our construction, we understand that we do not write on a blank slate.[153] We are cognizant that we depart from Judge Pisano's construction in some aspects, and agree with it in others. As discussed above, the major disagreement in this matter concerns the term "trihydrate" and its meaning to the POSA at the time of the invention. For the following reasons, the Court finds that the POSA would understand the term "trihydrate" to indicate a crystalline form. The Court declines to adopt the additional purity limitations sought by Perrigo and Mylan because the Court finds no basis to do so.

We being our analysis by focusing on the additional purity limitations sought by Perrigo and Mylan in their proposed constructions, namely "substantially free from magnesium salts of R-omeprazole and other forms of magnesium salts of S-omeprazole" (Perrigo) and "substantially pure" (Mylan). Neither phrase appears in the language of any claim of the '085 or '070 Patents. The language appears in the specification and the prosecution history.

[153] As discussed in Section I.C.2, supra, Judge Pisano previously construed this term to mean "a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-omeprazole," the same construction AstraZeneca advocates for here. He rejected the construction proposed by the defendants, "a trihydrate of a magnesium salt of S-omeprazole containing three molecules of water per molecule of magnesium salt of S-omeprazole in a unit cell of the crystal lattice that is substantially free from magnesium salts of R-omeprazole and other prior art forms of magnesium salts of S-omeprazole including S-omeprazole dihydrate and amorphous forms," finding that there was no basis to import the limitations sought by the defendants in that case into the claim language.

Perrigo and Mylan respectively argue that these phrases in the written description and prosecution history amount to disavowal and disclaimer.[154] The Court does not agree. A disclaimer or disavowal of claim scope must be clear and unmistakable, requiring "words or expressions of manifest exclusions or restriction" in the intrinsic record. Teleflex, Inc. v. Ficosa N. Am. Corp., 299 F.3d 1313, 1327 (Fed. Cir. 2002).

The language Mylan refers to in the written description is far from a clear and unmistakable disavowal. (See '070 Pat., col. 2, ll. 18-20 ("It is an object of the present invention to provide **substantially pure** magnesium salt of S-omeprazole trihydrate. . . ." (emphasis added)).) Setting forth "objects of the present invention" in the written description is "a common practice in patent drafting." Pacing Techs., LLC v. Garmin Int'l, Inc., 778 F.3d 1021, 1025 (Fed. Cir. 2015). "The characterization of features as 'an object' or 'another object,' or even as a 'principal object,' will not always rise to the level of disclaimer." Id. There is no statement that the invention (i.e., the magnesium salt of S-omeprazole trihydrate) is required to or must accomplish this stated "object." As AstraZeneca points out, the drafter may have been referring to the processes for obtaining the compound, not the compound itself. (See dkt. 48 at 20-21.) There is no clear and unmistakable disavowal that would require this limitation to be imported into the meaning of this claim term.

The language Perrigo identifies in the written description is similarly insufficient to find disclaimer:

[154] (See, e.g., Perrigo action, dkt. 48 at 13-15, 20, 26-27.)

> The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is **substantially free from magnesium salts of R-omeprazole.** The magnesium salt of S-omeprazole trihydrate obtained according to the present invention is **also substantially free from other forms of magnesium salts of S-omeprazole, such as the corresponding magnesium salt compounds described in the prior art, and dehydrates used in the preparation of the trihydrate compound** according to the present invention.

('070 Pat., col. 2, ll. 34-43 (emphasis added).) Nothing in these statements constitutes a mandatory claim limitation that must be read into the claims. The Court does not read this written description as clearly and unmistakably requiring that the invention, i.e., the magnesium salt of S-omeprazole trihydrate, include these limitations. Again, the drafter may have been referring to the processes for obtaining the compound. Claim 1 of the '085 Patent and Claim 1 of the '070 Patent are compound claims. Each claim, on its face, does not include such limitations.

In addition, the Court does not read the prosecution history as clearly and unmistakably requiring the importation of these limitations. In determining whether a clear and unambiguous disclaimer attaches to particular claim language, it is important to consider the statements made by the applicant both in the context of the entire prosecution history and in the then-pending claims. See Ecolab, Inc. v. FMC Corp., 569 F.3d 1335, 1342 (Fed. Cir. 2009) ("Even if an isolated statement appears to disclaim subject matter, the prosecution history as a whole may demonstrate that the patentee committed no clear and unmistakable disclaimer."). In the context of the overall prosecution histories of the '085 and '070 Patents, the isolated statements identified by Perrigo do not meet the high standard for prosecution disclaimer to attach. The Court

declines to import these limitations into the claims based on the written description or the prosecution history.

The Court also disagrees with Perrigo and Dr. Buckton that the written description defines the term "the magnesium salt of S-omeprazole trihydrate" as a "bulk product." That term does not appear anywhere in the written description or the claims, as Dr. Buckton readily admits. Cf. SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1338-1339 (Fed. Cir. 2005) (finding claim not limited to commercially significant quantities.) The Applicants never discussed the invention in terms of amount or quantity, other than providing a "yield" in Examples 1 and 7. (See '070 Pat., col. 5, ll. 21-24; col. 9, ll. 45-48.) Thus, the Court will not import any such limitation into the claims at issue.

We now focus on the term trihydrate and its meaning to the POSA at the time of the invention. We begin our analysis by focusing on the intrinsic evidence, starting with the claims themselves. The term "the magnesium salt of S-omeprazole trihydrate" appears in multiple claims. It appears in claim 1 of the '085 Patent with additional language that limits that claim to a specific crystalline form embodiment. (See dkt. 39 at 8.) It appears alone in claim 1 of the later issued '070 Patent, without this language or any further limitation. It appears in claim 2 of the '070 Patent, with reference to the X-ray diffractogram shown in Figure 1 of that patent, which is also indicative of a specific crystalline form embodiment. AstraZeneca argues that claim 1 of the '085 Patent and claim 1 of the '070 Patent have a different scope. AstraZeneca also argues that claims 1 and 2 of the '070 Patent have a different scope. Based on the difference in scope, AstraZeneca contends that the doctrine of claim differentiation counsels against a

crystallinity limitation associated with the term trihydrate. (See dkt. 39 at 8-10; dkt. 48 at 18-19, 28.)

Claim differentiation "only creates a presumption that each claim in a patent has a different scope; it is not a 'hard and fast' rule of construction." Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1376 (Fed. Cir. 2001) (citing Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed. Cir. 1998)). "However, the doctrine of claim differentiation cannot broaden claims beyond their correct scope, determined in light of the specification and the prosecution history and any relevant extrinsic evidence." Multiform Desiccants, Inc. v. Medzam, Ltd., 133 F.3d 1473, 1480 (Fed. Cir. 1998).

The Court finds that claim 1 of the '070 Patent is broader than dependent claim 2 of the '070 Patent. Claim 1 of the '070 Patent is also broader than claim 1 of the '085 Patent.[155] A comparison of these claims alone reveals as much. Both claim 1 of the '085 Patent and claim 2 of the '070 Patent include limitations beyond that of claim 1 of the '070 Patent. However, the doctrine of claim differentiation cannot broaden the term "the magnesium salt of S-omeprazole trihydrate" beyond its correct scope. Recognizing that claim 1 of the '070 Patent must be broader than claim 2 of the '070 Patent, as well as

[155] The Federal Circuit has acknowledged that two claims with different terminology can define the exact same subject matter. See Tandon Corp. v. U.S. Int'l Trade Comm'n, 831 F.2d 1017, 1023 (Fed. Cir. 1987). As discussed in Section II.B.1.b, supra, the parties have explained that Figure 1 and Table 1 (which is incorporated into claim 1 of the '085 Patent) depict the same test data. Although claim 1 of the '085 Patent and claim 2 of the '070 Patent use different terminology, these claims define the same subject matter, a specific embodiment of a compound that when analyzed would produce the X-ray diffractogram shown in Figure 1 and the major peaks listed in Table 1.

claim 1 of the '085 Patent, the task confronting the Court is to determine the correct scope of that term, specifically the meaning of the term trihydrate. AstraZeneca contends that the term trihydrate should be given its customary and ordinary meaning, which it argues is a chemical compound with three molecules of water. (See dkt. 39 at 12.) All of the defendants contend that a trihydrate was understood by the POSA to mean a crystalline form.

The defendants argue that certain statements in the written description suggest the trihydrate is crystalline. (See, e.g., dkt. 38 at 13-14.) For example, the written description states that "[t]he compound of the invention is characterized by being highly crystalline, i.e., having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art." ('070 Pat., col. 2, ll. 52-55.) It also states that "[t]he compound of the invention may also be characterized by its unit cell." (Id., col. 2, ll. 63-64.) AstraZeneca argues that these statements do not suggest the trihydrate must always be crystalline, and instead refer to characteristics of various embodiments. (See dkt. 39 at 10-11.) The Court agrees with AstraZeneca on this point. These statements, as well as others, emphasize that the compound may exhibit favorable characteristics. Similar statements state this exactly: "[t]he compound of the invention is **advantageous** because it is more stable than the corresponding magnesium salt compounds in the prior art and is therefore easier to handle and store." ('070 Pat., col. 2, ll. 26-28.) "A description of characteristics does not redefine a compound with an established and unambiguous structural definition." SmithKline Beecham Corp. v. Apotex Corp., 403 F.3d 1331, 1339 (Fed. Cir. 2005). Moreover, where a patent includes a long list of

different characteristics or embodiments that correspond to features positively recited in one or more claims, it seems unlikely that the Applicants intended for each claim to be limited to all of these characteristics. See '085 Pat., claims 2, 3.

The defendants also emphasize that the only two examples provided in the specification of the trihydrate form yield a crystalline product, suggesting that only a crystalline form was contemplated. (See, e.g., dkt. 38 at 14.) This may be true, but the Federal Circuit has repeatedly held that it is "not enough that the only embodiments, or all of the embodiments, contain a particular limitation" to limit claims beyond their plain meaning. Thorner v. Sony Computer Entm't Am. LLC, 669 F.3d 1362, 1366 (Fed Cir. 2012); GE Lighting Sols., LLC v. AgiLight, Inc., 750 F.3d 1304, 1309 (Fed. Cir. 2014). The Court declines to limit this term based on the statements made in the specification.

The written description does not provide a definition for the term trihydrate. However, AstraZeneca argues that it does provide an explanation that hydrates can exist in crystalline as well as amorphous forms. (See dkt. 48 at 13-14.) Specifically, AstraZeneca points to the following language:

> The compound of the invention is characterized by being highly crystalline, i.e., having a higher crystallinity than any other form of magnesium salt of S-omeprazole disclosed in the prior art. With the expression "any other form" is meant anhydrates, hydrates, solvates, and polymorphs or amorphous forms thereof disclosed in the prior art. Examples of any other forms of magnesium salt of S-omeprazole includes, but are not limited to anhydrates, monohydrates, dehydrates, sesquihydrates, trihydrates, alcoholates, such as methanolates and ethanolates, and polymorphs or amorphous forms thereof.

('070 Pat., col. 2, ll. 44-62.) The Court disagrees. This language is far from clear. It does not unequivocally suggest such a teaching or the understanding of the Applicants. The written description itself fails to describe the bounds of the term trihydrate.

Turning to the prosecution history, the defendants point to various excerpts from the file histories of both patents and contend they support the notion that the trihydrate was understood to be crystalline. (See dkt. 38 at 14-15.)[156] Most citations are to the file history of the '085 Patent. Many of the statements cited by the defendants are the same or similar to the statements found in the written specification. In fact, some are direct quotes from the specification. AstraZeneca interprets the prosecution history as clear evidence that the '070 Patent has a broader scope than the crystalline trihydrate of claim 1 of the '085 Patent. (See dkt. 39 at 11-12; dkt. 48 at 23-26.) AstraZeneca further argues that statements made in the '070 prosecution history do not support the defendants' views regarding crystallinity and that the defendants put too much emphasis on the prosecution history of the '085 Patent.

As explained above, we do not disagree with AstraZeneca with respect to the difference in scope of claim 1 of the '070 Patent and claim 1 of the '085 Patent. The USPTO acknowledged a difference in scope when it withdrew the statutory double patenting rejection during the prosecution of the '070 Patent. See n. 73 and accompanying text, supra. While some statements in the prosecution history may be viewed as suggesting the trihydrate is crystalline, other statements do not. With respect

[156] (See Perrigo action, dkt. 50 at 19-20.)

to the '070 Patent's file history, there is a lack of any conclusive statements regarding crystallinity.

After reviewing the specification and prosecution histories in detail, the question of whether the term "trihydrate" was understood by the POSA to connote a crystalline form is left unanswered. As a result, the Court must turn to the extrinsic evidence.

After thoroughly reviewing the extrinsic evidence, the Court finds the testimony and exhibits of Andrx's expert, Dr. Zaworotko most persuasive. He opined that the term "trihydrate" was understood by the POSA to refer to a crystalline form that has three water molecules, entrapped in its crystal lattice, for every molecule of compound. Each of the texts he cited, (see n. 111, supra), were consistent with the definition he provided and evidenced a common understanding of the term at the relevant time. Two of these texts were authored by AstraZeneca's expert, Dr. Byrn. Dr. Byrn's writings from 1994 and 1995 made clear distinctions between hydrates and amorphous forms on the basis of crystallinity. See n. 113, supra. Based on these references, the Court is persuaded that the POSA would have understood the term "trihydrate" to mean a crystalline form.

The references advanced to the contrary by Dr. Byrn were not persuasive. The dictionary definitions relied on by Dr. Byrn are too broad. See n. 91, supra. Both definitions explain that there were three waters, but do not provide any detail regarding the form in which those waters take. Thus, the dictionary definitions fail to properly define the term "trihydrate" as it would be understood by the POSA looking at these pharmaceutical patents-in-suit. The references Dr. Byrn initially cited to support the notion that amorphous hydrates were known at the time of the invention were well after

the May 30, 1997 priority date, and thus were not evidence of what was known at the time of the invention. (See n. 89, supra.) The six additional references he cited fail to conclusively establish that amorphous hydrates were known at the relevant time. (See n. 90, supra.)

Additionally, the Court does not agree with Dr. Byrn's assertions that solid state materials exist on a continuum of amorphous and crystalline material. See n. 95, supra. His prior writings directly contradict this position. See n. 113, supra. His prior writings also directly contradict his characterization of a hydrate as having some structure that "can bind water in a regular way." See n. 88 and accompanying text, supra.

As discussed above, the doctrine of claim differentiation cannot broaden the claim beyond its correct scope. Here, it cannot transform the meaning of a "trihydrate" to encompass amorphous forms. Yet, claim 1 of the '070 Patent must be broader than claim 2 of the '070 Patent (and claim 1 of the '085 Patent). The Court finds that it is. As explained by Dr. Zaworotko, compounds existing in more than one crystal structure are "polymorphic," which means the compound can crystallize into more than one distinct crystal structure through different crystal packing motifs. Thus, claim 1 of the '070 Patent may cover all crystalline polymorphs of S-omeprazole magnesium trihydrate. Dr. Byrn's writings are consistent on this point. See n. 88, supra. Claim 1 of the '070 Patent is broader than both claim 1 of the '085 Patent and claim 2 of the '070 Patent, which are both limited to a particular crystalline polymorph of that trihydrate. Construing the term trihydrate to connote a crystalline form does not violate the doctrine of claim differentiation.

After independently assessing the claims, the specification, the prosecution history, and the relevant extrinsic evidence, the Court finds Andrx's construction to be most accurate in declaring the meaning of this claim term as of the priority date in 1997.

In adopting Andrx's proposed construction for this term, the Court must be cognizant of the crystalline definition of prior related cases.[157] Judge Pisano previously construed the term "in crystalline form" found in claims 3, 6, 9, and 12 of the related '872 Patent to mean "at least some of the magnesium salt of esomeprazole present is in a solid with a repeating pattern of atoms or molecules of the constituent chemical species," adopting AstraZeneca's proposed construction. AstraZeneca AB v. Dr. Reddy's Laboratories, Ltd., No. 05-5553, 2010 WL 1981790, at *3 (D.N.J. May 18, 2010). The defendants' construction, "a solid in which the constituent molecules are arranged in an orderly, repeating pattern or lattice in all three spatial dimensions," was rejected. Id. The disagreement between the parties in that case was the degree of crystallinity the term required, i.e., the compound having "some" degree of crystallinity versus the compound being entirely crystalline. Id. The Court resolved the dispute by relying on the intrinsic and extrinsic evidence, which suggested that a reference to "crystalline" material does not require that the material be completely or even mostly crystalline. See id. This issue is not before us. We were not asked to define the bounds of crystallinity as closely as Judge

[157] See, e.g., AstraZeneca AB v. Dr. Reddy's Laboratories, Ltd., No. 05-5553, 2010 WL 1981790 (D.N.J. May 18, 2010) (construing the term "in crystalline form" of the '872 Patent and the term "substantially crystalline form" of the '504 Patent); AstraZeneca AB v. Dr. Reddy's Laboratories, Inc., Nos. 11-2317, 11-4275, 11-6348, 2013 WL 1847639 (D.N.J. May 1, 2013) ((construing the term "in crystalline form" of the '872 Patent and the term "substantially crystalline form" of the '504 Patent).

Pisano did. The distinction the experts made in this case, and the one we have determined, was whether the term trihydrate was understood by the POSA to mean a crystalline form, or was broad enough to include amorphous forms. If we must define the bounds of crystallinity, we leave it for another day.

b. "characterized by the following major peaks in its X-ray diffractogram"

The Court adopts Perrigo's proposed construction and construes the claim term "characterized by the following major peaks in its X-ray diffractogram," as used in the specified claims of the '085 Patent, to mean "having each of the referenced major peaks in its X-ray powder diffractogram within normal experimental error."

The Court rejects AstraZeneca's proposed construction because it improperly conflates claim construction and infringement, two separate steps in the infringement analysis. See Conroy v. Reebok Int'l, Ltd., 14 F.3d 1570, 1572 (Fed. Cir. 1994) ("The determination of infringement requires a two-step analysis: (1) a proper construction of the claim to determine its scope and meaning, and (2) a comparison of the properly construed claim to the accused device or process." (citation omitted)). The focus at this stage of the proceedings is determining the scope and meaning of the claim terms, not what evidence, tests, or techniques may be used to prove infringement. To be clear, the Court does not express any view regarding how "normal experimental error" will affect the infringement analysis, whether a potentially infringing sample must be compared using XRPD to prove infringement, or whether infringement may be shown by another technique such as Fourier transform-infrared ("FT-IR") spectroscopy, Raman

spectroscopy, etc. (See '070 Pat., col. 2, ll. 44-47.) Those issues shall be addressed by the parties during the infringement portion of this case. For now, the Court's task is to determine the scope and meaning of this claim term.

Claim 1 of the '085 Patent claims a specific embodiment of a compound, "the magnesium salt of S-omeprazole trihydrate," and claims that specific embodiment by listing 13 major peaks of its X-ray diffractogram and their relative intensities. Those 13 major peaks are significant. For example, AstraZeneca explains that claim 1 is limited to a crystalline form because "[t]he tabulated peaks of claim 1 are indicative of crystalline material." (Dkt. 39 at 8.) AstraZeneca does not point to less than all 13 peaks in making this statement, but refers to the peaks collectively. (See id.)

The prosecution history of the '085 Patent reveals a similar usage of the 13 major peaks. For example, prior to amending claim 1 to include the limitations of claim 3, the Applicants stated in an Office action response that "[t]he claimed magnesium salt of S-omeprazole trihydrate is highly crystalline (**claim 2**) and is uniquely characterized by an X-ray powder diffractogram (**claim 3**) which distinguishes the claimed compound from any other form of the magnesium salt of S-omeprazole." (Dkt. 38-1 at 79-80 (emphasis in original).) Again, this statement does not refer to less than all 13 major peaks, it addresses them collectively. More importantly, this statement recognizes the significance of those peaks, to uniquely define the claimed compound in order to distinguish it from other forms, which is precisely what AstraZeneca has done in its papers. (See, e.g. dkt. 39 at 8.) The written description is consistent on this point. It explains that the compound of the invention may be characterized by the positions and intensities of the

major peaks and may be distinguished based on those characteristics. (See '070 Pat., col. 2, ll. 43-51.)

The parties acknowledge that the plain language of claim 1 indicates that the compound is characterized by the listed 13 major peaks. The Applicants elected to claim the compound of claim 1 by listing the 13 major peaks of its XRPD. The written description reveals that the XRPD depicted in FIG. 1 included "some additional very weak peaks," however the Applicants chose to omit those additional very weak peaks in Table 1, (see '070 Pat., col. 5, ll. 49-50) and also in claim 1. The additional very weak peaks could have been shown in Table 1 and claimed. They were not. Based on AstraZeneca's arguments, some of the 13 claimed major peaks shown in Table 1 and claimed could have been omitted. However, they were not. Further, the Applicants could have elected to characterize the compound by conventional FT-IR spectroscopy and claim it accordingly, however they did not. The Applicants had a variety of options, but chose to claim the compound in a certain way, and they must live with that choice. See Ethicon Endo-Surgery, Inc. v. U.S. Surgical Corp., 93 F.3d 1572, 1583 (Fed. Cir. 1996) ("[The Patentee] need not have included this limitation in its claims. Having done so, it must live with the language it chose.")

Although the Court construes claim 1 of the '085 Patent to have each of the 13 major peaks recited in the claim, the Court is mindful that construing the claims to require an exact match is too rigid. The parties and their experts all agree that there will be some range of normal experimental error in an X-ray powder diffractogram. For example, both Dr. Byrn and Dr. Atwood opined that relative intensities can vary to some

extent. The written description itself states that the "relative intensities are less reliable." ('070 Pat., col. 5 ll. 36-38.) For this reason, the Court rejects Andrx's proposed construction that would require each peak to fall within the exact range for relative intensity recited for that peak.

This Court's construction is not inconsistent with the construction Judge Pisano arrived at in AstraZeneca AB v. Dr. Reddy's Laboratories Inc., No. 11-2317 (JAP), 2013 WL 1847639 (D.N.J. May 1, 2013). As discussed in Section I.C.3, supra, Judge Pisano rejected the defendants' proposed construction ("having all of the referenced major peaks in its X-ray diffractogram") as too rigid, noting it failed to account for experimental error. However, Judge Pisano did not construe the term to include less than all of the recited 13 major peaks. Instead, he held that a perfect one-to-one relationship was not required because "the positions for the peaks may differ somewhat because of slight experimental errors." This Court's construction, accounting for normal experimental error, satisfactorily addresses Judge Pisano's concerns.

The Court rejects AstraZeneca's proposed construction because it focuses on the question of infringement, and not the meaning and scope of the claim. Much of AstraZeneca's briefing with respect to this claim term focuses on how the POSA would compare a diffractogram for a tested compound to a reference diffractogram to determine whether there is a match for purposes of infringement. (See dkt. 39 at 14-16 ("[A] person of ordinary skill in the art would recognize that while the S-omeprazole trihydrate at issue should be 'identifiable by reference' to a diffractogram including the listed peaks, an infringing magnesium salt of S-omeprazole trihydrate need not necessarily contain all of

the listed peaks."); dkt. 48 at 32-33 ("Peaks from other components in [a drug] product, such as excipients, may interfere with the peaks attributable to the compound").) Whether peaks from other excipients in a drug product would interfere with the peaks attributable to the compound is irrelevant at this juncture. The Court is not focused on a tested compound. Rather, the concern is defining the proper meaning and scope of this claim term.

After independently assessing the claims, the specification, the prosecution history, and the relevant extrinsic evidence, the Court finds Perrigo's construction to be most accurate in declaring the meaning of this claim term.

c. "represented by FIG. 1"

The Court adopts Perrigo's proposed construction and construes the claim term "represented by FIG. 1," as used in the specified claims of the '070 Patent, to mean "having an X-ray powder diffractogram that is the same as Figure 1 of the '070 Patent within normal experimental error."

Claim 2 references and incorporates Figure 1 of the '070 patent, which shows the pattern resulting from an XRPD analysis. See '070 Pat., Fig. 1. As discussed in Section II.B.3, supra, the level of sameness between Figure 1 required to identify the claimed compound is at the heart of the dispute with respect to this claim term.

The written description does not define "represented by." In fact, that term appears for the first and only time in the '070 Patent in claim 2. AstraZeneca argues that no construction is required and that the "plain meaning" of this term should govern, (see dkt. 39 at 17-18), but does not provide a clear basis for determining what the "plain

meaning" of this term was. AstraZeneca asks this Court to reject each of the defendants' proposed constructions as too rigid, arguing that they require an exact match with the X-ray powder diffractogram of Figure 1 to identify the claimed compound. AstraZeneca argues that the "complies with" language describing the analysis of the product yielded by Example 7, (see '070 Pat., col. 9, ll. 49-50), "makes it clear that 'represented by' does not mean 'the same as.'" (Dkt. 39 at 18.)

Contrary to AstraZeneca's assertion, the defendants' proposed constructions do not require an exact match with the X-ray powder diffractogram of Figure 1 to identify the claimed compound. Each of the defendants' proposed constructions, including the one adopted by this Court, accounts for normal experimental error. Construing this claim term to require an exact match, disregarding variances due to normal experimental error, would unduly narrow the scope of the claim.

AstraZeneca's argument pertaining to the "complies with" language reveals why AstraZeneca's proposed construction must be rejected. AstraZeneca argues that the "complies with" language demonstrates that an exact match is not required. However, AstraZeneca fails to suggest any level of sameness to satisfactorily identify the compound. The written description does not explain what is meant by "complies with." The entire sentence including that language states that "[t]he product [of Example 7] was analyzed using X-ray powder diffraction and the result complies with FIG. 1 and Table 1." ('070 Pat., col. 9, ll. 49-50.) The written description does not report any XRPD data or provide a diffractogram for the product of Example 7. There is simply no way to determine the level of sameness between Figure 1 and the results of Example 7's X-ray

powder diffraction analysis because the latter was omitted by the Applicants. AstraZeneca infers that they are different in some way, but there is nothing to suggest that they were not identical. Accepting AstraZeneca's construction would create ambiguity and leave the disagreement between the parties over this claim term unresolved.

The Applicants chose to claim the compound by referencing Figure 1, and they must live with that choice. See Ethicon Endo-Surgery, Inc., 93 F.3d at 1583. Figure 1 shows the pattern resulting from an XRPD analysis. The Applicants claimed a specific embodiment of a compound that when analyzed would produce a specific pattern. As all the parties and experts agree, that pattern would be subject to some variance within normal experimental error. As a result, the Court finds Perrigo's construction to be most accurate in declaring the meaning of this claim term.

Again, this Court's construction is not inconsistent with Judge Pisano's construction of this term. See AstraZeneca AB, 2013 WL 1847639, at *9. As discussed in Section I.C.4, supra, Judge Pisano rejected the defendants' proposed construction ("having an X-ray diffractogram the same as FIG. 1,") as too rigid. He viewed the defendants' proposed construction as requiring an X-ray diffractogram that is perfectly identical to Figure 1. Id. This Court's construction does not require perfect identity and accounts for normal experimental error.

III. CONCLUSION

For the reasons stated above, the Court hereby construes the claim terms as follows:

the claim term "the magnesium salt of S-omeprazole trihydrate," as used in the specified claims of the '085 and '070 Patents, means "the magnesium salt of S-omeprazole in crystalline form containing three molecules of water of crystallization per molecule of magnesium salt of S-omeprazole;"

the claim term "characterized by the following major peaks in its X-ray diffractogram," as used in the specified claims of the '085 Patent, means "having each of the referenced major peaks in its X-ray powder diffractogram within normal experimental error;" and

the claim term "represented by FIG. 1," as used in the specified claims of the '070 Patent, means "having an X-ray powder diffractogram that is the same as Figure 1 of the '070 patent within normal experimental error."

The Court will issue an appropriate order.

s/ Mary L. Cooper
MARY L. COOPER
United States District Judge

Dated: January 11, 2017